MAR 2 0 1930

VOLUME 23 NUMBER 3

ARCHIVES OF NEUROLOGY AND PSYCHIATRY

EDITORIAL BOARD

T. H. WEISENBURG, Philadelphia

SAMUEL T. ORTON, New York
H. DOUGLAS SINGER, Chicago
STANLEY COBB, Boston
E. W. TAYLOR, Boston
FREDERICK TILNEY, New York
ADOLF MEYER, Baltimore

MARCH, 1930

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, Jan. 7, 1919, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of Oct. 3, 1917, authorized Jan. 15, 1919.

CONTENTS OF PREVIOUS NUMBER

FEBRUARY, 1930. NUMBER 2

Forced Drainage of the Central Nervous System: Its Effect on the Blood and on the Cerebrospinal Fluid. Frank Fremont-Smith, M.D.; Tracy J. Putnam, M.D., and Stanley Cobb, M.D., with the Technical Assistance of Mary E. Dailey, A.B.; Margaret A. Carroll, AB., and Caroline Stephensen, A.B., Boston.

Tests for Sensibility: An Investigation Among Normal Subjects. Norvelle C. LaMar, M.D., Philadelphia.

Myeloradiculitis: A Clinical Syndrome, with Report of Seven Cases. Israel Strauss, M.D., and Abraham M. Rabiner, M.D., New York.

Paraplegia in Flexion, with Subacute, Combined Degeneration of the Cord. George W. Hall, M.D., and Edwin F. Hirsch, M.D., Chicago.

Bilateral Acoustic Neurofibromas: A Clinical Study and Field Survey of a Family of Five Generations with Bilateral Deafness in Thirty-Eight Members. W. J. Gardner, M.D., and Charles H. Frazier, M.D., Sc.D., Philadelphia.

Muscle Tone in Parkinsonian States. Lewis J. Pollock, M.D., and Loyal Davis, M.D., Chicago.

The Nature of von Recklinghausen's Disease and the Tumors Associated with It. Wilder Penfield, M.D., and Arthur W. Young, M.D., Montreal, Canada.

Myasthenia Gravis with Status Lymphaticus and Multiple Thymic Granulomas. Nicholas M. Alter, M.D., and Michael Osnato, M.D., New York.

Allergy as Cause of Epileptiform Convulsions. George L. Waldbott, M.D., Detroit.

News and Comment.

Abstracts from Current Literature.

Society Transactions:
Boston Society of Psychiatry and Neurology.
Philadelphia Neurological Society.
Thirteenth International Physiological Congress.

Book Reviews.

COPYRIGHT, 1930, BY THE AMERICAN MEDICAL ASSOCIATION

Archives of Neurology and Psychiatry

VOLUME 23 MARCH, 1930 NUMBER 3

THE CEREBELLUM

A NEW CLASSIFICATION OF THE LOBES BASED ON THEIR REACTIONS TO STIMULATION *

AUBREY T. MUSSEN, M.D.

BALTIMORE

PART I: A REVIEW OF THE NOMENCLATURE OF THE CEREBELLUM

In any discussion of the cerebellum, one of the greatest difficulties is to refer to the individual lobes in such a manner that the meaning is clear. Even among brain anatomists today there is confusion. The reason for this is that the various authorities have approached the study of the cerebellum from different angles, and have adopted individual nomenclatures to express their particular views.

The first effort to bring uniformity out of the early diverse descriptions of the cerebellum was made in 1895, when the "Basle Nomina Anatomica" [1] attempted to establish some order in the general confusion that existed in the terminology of the central nervous system. Among other things, the following classification of the cerebellar lobes was drawn up. As shown in table 1 the cerebellum was divided by the primary and secondary fissures into anterior, middle and posterior lobes. This classification has been generally accepted and has formed the basis of many of the subsequent descriptions.

A few years later, Elliot Smith [2] proposed a new terminology based on the study of the edentata and the marsupials, the great importance of which lay in the comparison made between the human cerebellum and that of other mammals. The primary and secondary fissures were again taken as the lines of division, the latter being selected from the posterior fissures on account of its greater constancy. As will be observed in table 2, the principal difference between this classification and that of the B. N. A. is in the description of the middle and posterior lobes of the hemisphere.

---

* Submitted for publication, May 1, 1929.

* Read at the Fifty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 27, 1929.

* From the Neurological Laboratory, Henry Phipps Psychiatric Clinic, Johns Hopkins Hospital.

1. Basle Nomina Anatomica, in Krause, W.: Handbuch der Anatomie des Menschen, Leipzig, 1905.

2. Smith, Elliot: The Morphology of the Human Cerebellum, Review of Neurology and Psychiatry, October, 1903.

In the vermis, the declive and the folium vermis become the lobus medius anterior; the tuber vermis, the lobus medius posterior.

In the hemisphere, the lobus quadrangularis anterior and posterior become the pars lunatus. The semilunaris superior and inferior are referred to as the pars pteroidea superior and inferior. The posterior lobe shows an important change in that the lobus biventralis is divided

TABLE 1.—*Cerebellar Lobes, According to the B. N. A. Classification, 1895*

	Sulci	Hemisphere	Vermis
Lobus ant.	Fiss. prim.		Lobus lingulae Lobus centralis Culmen monticuli
Lobus med.		L. quadrangularis ant. L. quadrangularis post. L. semilunaris sup.	Declive Folium vermis Tuber vermis Sul. prepyr.
	Fiss. secunda.	L. semilunaris inf.	Lobus pyramidis
Lobus posterior		L. biventralis L. tonsillaris L. paraflocc ularis L. flocc ularis	Lobus uvulae Lobus noduli

TABLE 2.—*Cerebellar Lobes According to Elliot Smith's Classification, 1899*

	Sulci	Hemisphere	Vermis
Lobus anterior	Fiss. prima		Lobus lingulae Lobus centralis Lobus culminis
Lobus medius		Pars lunatus Pars pteroidea sup.	Lobus medius anterior Lobus medius posterior Sul. prepyramidalis
	Fiss. secunda	Pars pteroidea inf.	Lobus pyramidis
Lobus posterior		Area parapyramidalis: Lobus gracilis; L. biventralis; L. tonsillaris	Lobus uvulae Lobus noduli
		Lobus paraflocc ularis Lobus flocc ularis	

into gracilis and biventralis. This is the first indication that this posterior lobe of the hemisphere was considered to be composed of three lobules—the lobus gracilis, the lobus biventralis and the lobus tonsillaris, the unity of which is suggested by being grouped together as the area parapyramidalis.

Then Bolk, in 1905,[3] after a comparative anatomic investigation of the mammalian cerebellums, proposed an entirely new nomenclature.

3. Bolk, Louis: Das Cerebellum der Säugetiere, Petrus Camper, 1905, vol. 3.

He considered that the fissura prima divided the cerebellum into an anterior and a posterior lobe. The anterior lobe, consisting of the lingula, the centralis and the culmen, he designates by the numerals 1, 2, 3 and 4. The posterior lobe was subdivided into the lobus simplex, which consists of unbroken folia extending from one hemisphere through the vermis into the other hemisphere. The lobus ansiformis, which comprised the bulk of the hemisphere, he represented by crus I, and crus II. In the posterior vermis the pyramis, uvula and nodule are shown as C 1, *b*, *a*. The remainder of the hemisphere includes the lobus paramedianus, which is made up of the gracilis, biventer and tonsil, the formatio vermicularis or paraflocculari and the flocculus.

TABLE 3.—*Cerebellar Lobes According to Bolk's Classification, 1902*

Sulci	Hemisphere		Vermis
Lobus anterior	1. 2 3. 4.		1. 2. 3. 4.
Fiss. prima			
Lobus posterior	Lobus simplex		Lobus simplex C. 2.
	Lobus ansiformis	Crus I.	C. 1.
		Crus II.	Fiss. secunda
	Lobus paramedianus	L. gracilis	b.
		L. biventralis	
		L. tonsillaris	a.
	Lobus paraflocc ularis		
	Lobus flocc ularis		

Horsley and Clarke's [4] description of the cerebellum of the cat (1905) was based principally on the work of Elliot Smith, but some suggestions of their own were added.

The primary and secondary fissures were retained as the lines of division separating the vermis into anterior, middle and posterior lobes. In the anterior and posterior lobes there was no change, but the middle lobe was divided into first, second, third and fourth lobules. The greatest difference is found in the description of the hemispheres. All the lobes are grouped together under the heading lobus medius. This is shown to be composed of five lobules. The first lies like a horseshoe behind the primary fissure. The second spreads out laterally into a series of folia arranged bipennately, and is called the anterior and posterior pennate lobes. The third lobe extends from the middle line laterally into the hemispheres, where it forms the two vertical paramedian lobes. The fourth lobe is the pyramis. But the lobus pyramis

4. Horsley, V., and Clarke, R. H.: On the Intrinsic Fibers of the Cerebellum, Its Nuclei and Its Efferent Tracts, Brain **28**:13, 1905.

of these authors included both the pyramis as well as the sigmoid arrangement of folia on the dorsal and posterior surface of the vermis in the cat, now known as the lobus medius posterior. The remainder of the lateral lobe is composed of the dorsal and ventral paraflocculus and the flocculus.

The next classification was made by Schäfer and Symington [5] in 1908. These authors made a number of radical changes. They took the sulcus horizontalis magnus as the important line of division and considered the cerebellum to be composed of an upper surface and an under surface. For the median lobes of the vermis they proposed the names clivus monticuli, folium cacuminis and tuber valvulae.

TABLE 4.—*Cerebellar Lobes According to the Classification of Horsley and Clarke, 1905*

	Sulci	Hemisphere	Vermis
Lobus anterior			Lobus linguiae Lobus centralis Lobus culminis
	Fiss. prima		
Lobus medius		1st lobule	1st lobule
		Lob. pennatus ant.	2nd lobule
		Lob. pennatus post.	
		Lob. paramedianus	3rd lobule
		Lob. parafloccularis dorsalis	
		Lob. parafloccularis ventralis	
		Lob. flocularis	4th lobule (lobus pyramis)
	Fiss. secunda		
Lobus posterior			Lobus uvulae Lobus noduli

The hemisphere contained the lobus lunatus posterior, the lobus posterior superior and the lobus posterior inferior, which was divided into the lobus semilunaris and gracilis. A small variation in the nomenclature is that the terms sulcus prepyramidalis and postpyramidalis are employed in the reverse order to that generally accepted.

In 1918, Ingvar [6] published the results of a careful ontogenetic and phylogenetic study of the cerebella in reptiles, birds and mammals. His description, which follows the B. N. A. classification closely, is modified by suggestions of Elliot Smith and Bolk. A particularly interesting decision of his own is added. He divided the cerebellum into three lobes, the primary fissure being again taken as the line of demarcation between the anterior and the middle lobes.

5. Schäfer and Symington, in Quain: Anatomy, 1908, vol. 3, p. 176.

6. Ingvar, Sven: Zur Phylo- und Ontogenese des Kleinhirns, Folia neurobiol., 1918, vol. 11.

The principal difference in this classification, and one of great importance, is found in the posterior lobe of the vermis. For, instead of limiting the middle lobe by the secondary fissure, i.e., the fissure between the pyramis and the uvula, the prepyramidal sulcus was taken as the line of division on account of its greater prominence in the carnivora. This is the first suggestion that the lobus pyramis should belong to the posterior division of the vermis. In birds, the pyramis was grouped with the uvula and nodule on account of the arrangement of the arbor vitae.

In the middle lobe of the vermis the lobus simplex of Bolk is retained, and with the folium vermis and the tuber vermis is included in the lobus medius medianus.

TABLE 5.—*Cerebellar Lobes According to the Classification of Schäfer and Symington, 1908*

Sulci	Hemispheres		Vermis
Upper surface	Frenulum lingulae Ala lobuli centralis Lobus lunatus anterior Lobus lunatus posterior Lobus posterior superior		Lobus longulae Lobus centralis Culmen monticelli Clivus monticuli Folium cacuminis
Sulcus horizontalis magnus			
Under surface	Lobus posterior inferior	L. semilunaris	Tuber valvulae Sul. postpyramidalis
		L. gracilis	
	Paraflocculus dorsalis	Lobus biventralis (Fiss. secunda)	Lob. pyramidis Sul. prepyramidalis
	Paraflocculus ventralis Flocculus	Tonsilla	Lob. uvulae Lob. noduli

The hemisphere contains anterior, middle and posterior lobes. The lobus anterior is similar to that described by Schäfer and Symington.[5] The lobus medius is composed of the lobus simplex, the lobus quadratus and the lobus semilunaris superior. The lobus posterior comprises the lobus semilunaris inferior, the gracilis, the biventer, the tonsil, the paraflocculus and the flocculus. This division of the semilunar lobes placing the superior division with the lobus medius, and the inferior division with the lobus posterior is open to criticism, partly on anatomic grounds, but particularly as it is against the results obtained on stimulation. These points will be considered in the discussion of the proposed classification.

In the description of the human cerebellum by Tilney and Riley[7] in 1923, the classification of Schäfer and Symington has been followed with but few modifications.

7. Tilney, F. W., and Riley, H. A.: Form and Functions of the Nervous System, 1923, New York, Paul B. Hoeber, Inc., pp. 429.

The great horizontal fissure is accepted as the dividing line which separates the cerebellum into superior and inferior lobes. The superior lobe includes the lingula, centralis, culmen, clivus and cacuminis. The tuber valvulae, pyramis, uvula and nodule form the inferior.

In the hemisphere, the divisions of the superior lobe are similar to those found in Quain, but in the inferior lobe the paraflocculus dorsalis is omitted and the gracilis is included.

In this classification, as in that of Schäfer and Symington, there is a reversion in the terminology applied to the fissures on either side of the lobus pyramis. The general rule is to refer to these according to their embryologic arrangement, as prepyramidal and postpyramidal, the latter being the secondary fissure. Here the view of Schäfer and Symington is followed, and one finds the postpyramidal between the

TABLE 6.—*Cerebellar Lobes According to the Classification of Ingvar, 1918*

	Sulci	Hemisphere	Vermis
Lobus anterior	Fiss. prima	Ala lobi centralis Ala lobi culminis	Lobus lingulae Lobus centralis Lobus culminis
Lobus medius	Sul. prepyramidalis	Lobus simplex Lobus quadratus Lobus semilunaris sup.	Lobus medianus: L. simplex; L. med. ant.; L. med. post.
		Lobus semilunaris inf.	Lobus pyramidis Fiss. secunda
Lobus posterior		Lobus gracilis Lobus biventralis Lobus tonsillaris Lobus paraflocculus Lobus floccularis	Lobus uvulae Lobus noduli

pyramis and the tuberis, and the secondary fissure becomes the prepyramidal.

Attention is also drawn to the support given by these authorities to the positions occupied by the fissura secunda and the sulcus postpyramidalis in the hemispheres. The former is placed between the lobus biventralis and the tonsil, the latter between the lobus gracilis and the biventralis. As this differs from the previous classification, it is mentioned to indicate that the position of these fissures in the hemisphere is not settled. This point will be further considered in connection with the grouping of the lobus semilunaris inferior.

Von Brun,[8] in his interesting monograph, discussed the cerebellum from the anatomic, physiologic and developmental standpoints. The investigations of a number of authorities on cerebellar stimulation are also reviewed. As these will be examined in a subsequent paper, they will not be considered here.

8. Von Brun, R.: Das Kleinhirn, Schweiz. Arch. f. Neurol. u. Psychiat. **7**:42, 1927.

In his classification of the lobes, the vermis is divided by the sulcus horizontalis magnus into a superior and an inferior division. The lateral lobes, consisting of the lobus quadrangularis, the lobus semilunaris superior and inferior, and the lobus cuneiformis are grouped together. The flocculus is separate. One gathers that this arrangement has been used more for the purpose of conveniently tabulating the stimulation results than as an indication of a special anatomic grouping.

In Kuhlenbeck's [9] description of the cerebellum, there is an interesting table in which a comparison is made between the division of the lobes, as suggested by Bolk and Ingvar on their comparative anatomic studies, and the old B. N. A. classification.

The cerebellum is considered as being composed of the lobus superior, the lobus posterior and the lobus inferior, the lines of division

TABLE 7.—*Cerebellar Lobes According to the Classification of Tilney and Riley, 1923*

	Sulci	Hemisphere	Vermis
Superior lobe		Frenulum lingulae Ala lobuli centralis Lob. lunatus anterior	Lobus lingulae Lobus centralis Lobus culminis
	Fiss. prima		
Sulcus horizontalis magnus		Lob. lunatus posterior Lob. posterosuperior	Lobus clivi Lobus cacuminis
Inferior lobe		Lobus postero-inferior {L. semilunaris inf. L. gracilis post. L. gracilis ant. Lobus biventralis	Lobus tuberis Lobus pyramidis
	Fiss. secunda		
		Lobus tonsillaris Lobus paraflocccularis Lobus flocccularis	Lobus uvulae Lobus noduli

being the sulcus superior posterior and the sulcus inferior posterior. The former refers to the sulcus horizontalis magnus, and the latter to the sulcus prepyramidalis.

It is to be regretted that there is evidently a tendency among later writers to break away from the old established—anterior, middle and posterior—divisions which the earliest experimenters, by both operation and stimulation, have shown to be so well founded.

Jakob [10] recently suggested another classification of the cerebellar lobes. In this, while the generally accepted division into anterior, middle and posterior is maintained and the composition of these lobes in the vermis follows that of Ingvar, the grouping of the lobes in the hemisphere is different.

9. Kuhlenbeck, H.: Vorlesungen über das Zentralnervensystem der Wirbeltiere, Jena, Gustav Fischer, 1927.

10. Jakob, A., in Handbuch der mikroskopischen Anatomie des Menschen, Nervensystem, Berlin, Julius Springer, 1928, vol. 4, p. 686.

The middle lobe comprises the bulk of the hemisphere, and includes all the lobes between the primary fissure and the paraflocculus; that is, in addition to the lobus simplex, the lobus quadratus, the lobus semilunaris superior and inferior; the lobus gracilis, the biventer and tonsil as well.

The posterior lobe is made up of the paraflocculus and the flocculus alone.

In addition, there is a "pars intermedia" which occupies "some portion" of the hemisphere between the vermis and the lateral lobes.

TABLE 8.—*Cerebellar Lobes According to Kuhlenbeck's Classification, 1927*

	Old Division (B. N. A.)		New Division (Bolk; Ingvar)
	Hemisphere	Vermis	
Lob. sup.	Vinculum lingulae	Lingula	Lobus anterior
	Ala lob. centralis	Lob. centralis	
	Lob. quadrangularis pars ant.	Culmen monticuli	
	Sulcus superior ant.		Sulcus primarius
	Lobus quadrangularis pars post.	Declive monticuli	Lobus simplex
	Sul. superior posterior		
Lob. post.	Lob. semilunaris sup.	Folium	Lob. medius: Lobus medius medianus; Lobul. ansiformis; Lobulus anso-paramedianus
	Lob. semilunaris inf.	Tuber	
	Sul. inferior posterior		Sulcis prepyramidalis; Sul. Lobus paramedianus
Lob. infer.	Lob. gracilis		Lobus postmedianus; Sul. Parameid. Sul. paraflocculus
	Lob. biventer	Pyramis	
	Lob. tonsillaris	Uvula	
	Lob. flocculus	Nodulus	Lob. post. Floeculus Paraflocculus

It is difficult to understand on what principle this classification is based. It comes opportunely, nevertheless, as it shows the uncertainty that exists regarding the grouping of the lobes, and serves to emphasize the importance of having this question of the cerebellar nomenclature thoroughly discussed.

In Winkler's [11] consideration of the cerebellar lobes, the plan of Schäfer and Symington has been closely followed. The sulcus horizontalis magnus is accepted as the principal fissure, and the cerebellum is divided into a pars dorsalis and a pars ventralis.

11. Winkler, C.: Manuel de neurologie; Opera omnia, Haarlem, de Erven F. Bohn, 1927, vol. 8, p. 119.

As is usual with most authorities, some modification is brought in. Here, fortunately, it concerns the lateral course of the sulcus prepyramidalis, about which there are so many different opinions.

In Schäfer and Symington's description, as in that of Tilney and Riley, the prepyramidal sulcus (postpyramidal of these authors) divides the lobus gracilis from the lobus biventralis. Ingvar shows it as separating the lobus semilunaris superior from the lobus semilunaris inferior. With Winkler the lobus biventralis includes the gracilis, and in his classification it will be seen that the prepyramidal sulcus marks the division between the lobus biventer and the lobus lunatus inferior (i. e., the lobus semilunaris inferior).

This is the only instance that I am familiar with in which the prepyramidal sulcus is shown to separate the lobus semilunaris inferior

TABLE 9.—*Cerebellar Lobes According to Winkler's Classification, 1927*

Vermis	Sulci	Hemispheres
	Pars Dorsalis Cerebelli	
1. Lingula	Sulcus postlingualis	Vinculum lingulae
2. Lobulus centralis	Sulcus postcentralis	alae lobuli centralis
3. Culmen	Sulcus superior anterior (sulcus primus)	lobulus quadratus anterior
4. Declive	Sulcus superior posterior	lobulus quadratus posterior
5. Folium cacuminis		lobulus lunatus superior
	Pars Ventralis Cerebelli	
6. Tuber vermis	Sulcus horizontalis magnus	lobulus lunatus inferior
7. Pyramis	Sulcus prepyramidalis; sulcus inferior posterior	lobus biventer
8. Uvula	Sulcus secundus; sulcus inferior anterior	tonsilla
9. Nodulus	Sulcus uvulo-nodularis	flocculus formatio

from the (gracilis) biventer and tonsil, and in so doing it offers a precedent for the position which this sulcus is described as following in my classification.

In the preceding brief review, the idea has been to bring together only those classifications which have been generally accepted, in order that by comparison the remarkable variety of opinions held by the leading authorities could be demonstrated. In some, as has been shown, the primary and secondary fissures, in others the primary and prepyramidal fissures, have been accepted, and the cerebellum divided into anterior, middle and posterior lobes. Then the primary fissure alone has been considered, the lobes of the cerebellum being arranged into anterior and posterior groups. In the view of others the most important landmark is the great horizontal sulcus, which separates the cerebellum into an upper surface and an under surface or a superior and an inferior portion.

But there can be little doubt that the soundest basis of cerebellar classification is that which considers an anterior, a middle and a posterior lobe of both vermis and hemispheres.

Flourens,[12] in 1864, laid the foundation for such a division. He showed clearly that the vermis in its anterior region controlled mechanisms for the maintenance of forward balance. The loss of backward balance was placed in the posterior vermis, for injury in this region caused the animal to fall supine; and a lesion in the hemisphere produced disturbance in the lateral balance. The stimulation experiments of Ferrier,[13] about twenty years later, confirmed these observations. In addition, a middle region between the anterior and posterior vermis was reported which on stimulation produced a turning of the head and eyes toward the side excited.

The result of these early experiments was to demonstrate that the vermis contained three distinct regions—an anterior, for the maintenance of forward balance; a posterior for the control of backward balance, and a median for the lateral movements of the head and eyes. But beyond the fact that the cerebellum had been shown to be associated with the maintenance of forward, backward and lateral balance, nothing was known. How these reactions were brought about was of course not understood.

In the past, when various divisions and different names were employed to designate the subdivisions of the cerebellum, it made little difference as only an anatomic arrangement of the lobes was indicated. But when from experimental and clinical experience function began to be assigned to the separate lobes and these were referred to by several classifications, it became more perplexing. And finally, when it was found that the cerebellar lobes of the cat and the monkey gave definite responses to stimulation and it became necessary to compare the reactions, the confusion caused by referring to similar lobes in different cerebella by various names suggested the desirability of a nomenclature that would be of general application, not only to the cat and the monkey but also to man. For it seems reasonable to argue that if the reactions obtained from the various cerebellar lobes of the rabbit are practically similar to those found in the cat, and those in the cat correspond to the results obtained in the monkey, the reactions observed in the monkey should be accepted as indicating the possible function of similar lobes in the human cerebellum, in the same manner as the reactions of the motor cortex of the monkey were eventually accepted as representing the function of the motor cortex in man.

---

12. Flourens: Recherches expérimentales sur les propriétés et les fonctions du système nerveux, 1842, et. 2.

13. Ferrier, D.: Functions of the Brain, 1876.

With this in view and remembering the great confusion that already exists, I have carefully examined the cerebella of the cat, the monkey and man. After many drawings in which the individual folia and sulci of these different cerebella were clearly represented, the great similarity between them was evident.

The difficulty, though, was to find a method by which it would be possible to demonstrate the remarkable resemblance that existed, not only by reason of their anatomic relations but also by their cortical activities, a method in which the arrangement of the folia comprising the lobes would be clearly shown as well as the position of the fissures and sulci. For it was held that the division of the lobes according to the stimulation results should agree with their anatomic positions.

Written descriptions are unsatisfactory for quick comparison, as they require too much study. Marked photographs are more helpful but leave much to be desired, as only one view at a time can be shown, and even in a series it is difficult to follow the relations of the various lobes and fissures.

Eventually the plan was adopted of representing the lobes of the vermis, folium by folium, in a column. Opposite these the lobes of the hemisphere were placed, the number and arrangement of their surface folia being carefully shown, i. e., the lobes of the cerebellum were spread out so that all of them could be represented on a flat surface. Drawings have been, of course, frequently used in descriptions of the cerebellum, but these were largely diagrammatic to illustrate in a general way the arrangement of the main lobes and fissures. The method followed here is entirely different, in that each surface folium of the cerebella of the cat and the monkey is represented, and by spacing, the position of the fissures and sulci is clearly indicated. In the human cerebellum, owing to the great number and complexity of the folia, only the outline of the lobes is shown.

This method, while time absorbing, has proved of great assistance; for it has made it possible to depict in a clear and simple manner the arrangement of the lobes, the number of the folia in each and the fissures and sulci that divide them, besides drawing attention to interesting peculiarities in structural arrangement. The great resemblance between homologous lobes in the different cerebella will be readily observed.

PART II: HOMOLOGY BETWEEN THE LOBES OF THE CAT, THE MONKEY AND MAN

In the classification that is now presented for consideration, the homology between the lobes of the cat, the monkey and man is emphasized. Though my classification is based principally on the B. N. A. terminology, those of Elliot Smith, Bolk, Ingvar, Schäfer and Symington, and Tilney and Riley have been carefully considered. And when

some uncertainty has arisen as to the grouping of a particular lobe, owing to the indefinite course of certain fissures in the hemisphere, the position of the lobe has been determined by the character of its reactions to stimulation. For as these reactions occur in those muscles which are situated opposite the lobe that gives rise to them, the results of stimulation are helpful in determining whether a lobe belongs to the anterior, the middle or the posterior group.

It may appear that the question of the grouping of a lobe should not be difficult to decide. But there are two particular lobes about which different opinions are held, on account of the uncertainty that exists regarding the location of the sulcus prepyramidalis and the fissura secunda in the hemisphere. These are the lobus pyramis and the lobus semilunaris inferior. In all classifications in which the cerebellum is divided into anterior, middle and posterior lobes the pyramis has been included in the middle lobe, with one exception; and the lobus semilunaris inferior has been grouped with the posterior lobes. The reactions of these lobes to stimulation indicate that both have been incorrectly placed, that the pyramis should form part of the posterior vermis, and the semilunaris inferior should belong to the lobus medius of the hemisphere.

In the description of the classification given in table 10, the discussion will be confined to the grouping of the lobes; the consideration of their reactions to stimulation; the influence this has on determining their position, and the examination of the relations of the secondary fissure and the prepyramidal sulcus in the hemisphere about which there is considerable controversy.

In table 10 the cerebellum is shown as being divided into anterior, middle and posterior lobes by the primary fissure and the sulcus prepyramidalis.

The lobus anterior of the vermis and hemisphere is the only division that has not changed since the cerebellar lobes were classified. It is composed of the lingula, the centralis and the culmen in the vermis, the hemispheral part being formed of their lateral extensions, when present. The lobe rests anteriorly on the superior medullary velum, and is bounded posteriorly by the primary fissure.

On stimulation, the lingula gives reactions in the larynx and pharynx as indicated by swallowing movements and by a sharp cry; the centralis and the culminis show responses in the posterior neck muscles, the head being pulled backward and the eyes turned up, a center for the control of forward balance being thus indicated.

The lobus medius of both vermis and hemisphere shows a number of changes. In the vermis, instead of the lobus clivi or its synonym the declive monticuli, the lobus simplex of Bolk is employed as being more appropriate to the cat and monkey, yet equally applicable to man.

For the same reason, instead of the folium vermis and the tuber vermis —their equivalents being the lobus cacuminis and the tuberis—the lobus medius anterior and the lobus medius posterior of Elliot Smith are adopted. In the hemisphere the lobus medius is divided into three groups, according to their reactions: (1) An anterolateral group composed of the lobus simplex and the lobus quadratus. On stimulation these show reactions in the posterolateral neck muscles, the head being drawn backward and sideways. (2) The lateral group of folia which forms the lobus semilunaris superior, stimulation of which produces contraction in the lateral neck muscles, drawing the head toward the shoulder. (3) The posterolateral, which is represented by the lobus

TABLE 10.—*Cerebellar Lobes According to Mussen's Classification, 1929*

	Sulci	Hemisphere		Vermis
Lobus anterior	Precentralis	Frenulum lingulae		Lobus lingulae
	Postcentralis	Ala lobi centralis		Lobus centralis
		Ala lobi culminis		Lobus culminis
Fiss. prima				
Lobus medius	Postsimplex	Lobus simplex		Lobus simplex
	Horizontalis magnus	Lobus quadratus		L. medianus anterior
	Intersemilunaris	L. semilunaris sup.		L. medianus posterior
		L. semilunaris inf.		
Sulcus prepyramidalis				
Lobus posterior	Postgracilis	Lob. gracilis	Lobus paramedianus	L. pyramis
		Lob. biventralis		
	Fiss. secunda	Lob. tonsillaris		
	S. uvulonodularis			L. uvulae
	S. paraflocculus			L. noduli
		Lob. paraflocculari		
		Lob. flocculari		

semilunaris inferior, excitation of which causes reactions in the anterolateral neck muscles, opening the jaw and drawing the head forward and laterally. The posterior boundary of the lobus medius in both vermis and hemisphere is the sulcus prepyramidalis.

The inclusion of the lobus semilunaris with the lobus medius and the given position of the sulcus prepyramidalis laterally will probably be questioned. In both the B. N. A. and Elliot Smith's classifications this lobe is included with the lobus medius, but the limiting fissure is shown to be the fissura secunda, which in the vermis lies between the pyramis and the uvula. Ingvar, who also divided the cerebellum into anterior, middle and posterior lobes, places the lobus semilunaris inferior with the posterior group, because he considers that the sulcus prepyramidalis in its lateral extension lies between the semilunaris superior and the semilunaris inferior.

On account of this supposed position of the prepyramidal sulcus the semilunar lobes are divided, the superior being grouped with the lobus medius and the inferior with the lobus posterior. But the position of the sulcus prepyramidalis in the hemisphere is not definitely settled, for in the opinion of Schäfer and Symington—and they are supported by Tilney and Riley—the lateral extension of this sulcus lies between the lobus gracilis and the biventralis (though these authorities refer to this sulcus as the postpyramidal).

Confronted by these different opinions as to the position of the prepyramidal sulcus, the question of the grouping of the lobus semilunaris inferior was difficult to decide on anatomic grounds. But according to its reaction to stimulation, it clearly formed part of the lobus medius of the hemisphere. For, as has been shown, when the lobe was excited, the anterolateral neck muscles responded. And as this balanced the reactions of the lobus simplex and the quadratus and was associated with those of the lobus semilunaris superior, it was considered that the lobus semilunaris inferior should be grouped with the median division, which would then include all the lobes that were related to the anterolateral, the lateral and the posterolateral muscles of the neck, rather than with the posterior division which is concerned with the muscles of the limbs and back.

The position of the prepyramidal sulcus in the hemisphere was therefore changed from the former position ascribed to it by various authorities to one lying between the lobus semilunaris inferior and the lobus gracilis. This agrees with Winkler's classification.

It is true that in the cat's cerebellum the course of the sulcus prepyramidalis is somewhat unusual. But as there is no definite division between the upper and the median lobules of the paramedian lobe no other course was possible. On the other hand, in the cerebella of both monkey and man, if the lobes are well separated and carefully examined, the prepyramidal sulcus can be followed clearly from the division between the pyramis and the uvula into the sulcus lying between the lobus semilunaris inferior and the lobus gracilis. From this, it would appear that the described position of the prepyramidal sulcus was well supported on anatomic grounds.

Another disputed point is the position of the fissura secunda in the hemisphere.

In the B. N. A. classification, the secondary fissure is shown between the semilunaris inferior and the gracilis. Elliot Smith, Ingvar and Bolk agree with this, though the former refers to the lobus semilunaris inferior as the pars pteroidea inferior, and the latter as crus II. On the other hand, Schäfer and Symington, Tilney and Riley, and Winkler consider that the secondary fissure separates the biventralis from the tonsil. It is obvious from this that it has not been possible

to determine definitely, either embryologically or anatomically, just what is the real position of this fissure.

In the present comparative study of the cat, monkey and man the course of the secondary fissure in the hemisphere is clearly observed to follow the course between the biventralis and the tonsil. In the cat, the division between the lower and middle lobules of the paramedian lobe is directly opposite the fissura secunda which separates the pyramis from the uvula. It is natural, therefore, to consider that this fissure would pass straight laterally, and consequently would lie between the median and lower lobules of the paramedial lobe, or in other words, between the biventral lobe and the tonsil.

In the monkey, both the median and the posterior lobes are much larger, particularly in their lateral parts. The result is that all the folia are pushed downward, pivoting from their median portions; so that while the median portions of the folia forming the gracilis, biventer and tonsil still retain the same relative positions to the lobes of the vermis, as in the cat, the lateral regions of these folia are at an angle of 45 degrees.

In man, there is still greater change owing to the enormous increase of the anterior middle and posterior lobes. The gracilis and the biventer have developed laterally and posteriorly, with the result that the tonsil has been twisted forward and inward, being almost embedded in the biventralis. But the dorsal border of the tonsil is still opposite the uvula, and it is still possible for the fissura secunda to pass directly lateral from between the pyramis and the uvula. After crossing the stem of the tonsil the secondary fissure enters between the tonsil and the biventralis and taking a sharp ventral turn at an angle of 90 degrees, it curves forward to end in the hilus cerebelli, against the body of the flocculus.

In old descriptions this division between the tonsil and the lobus biventralis was referred to as the sulcus pretonsillaris, the sulcus posttonsillaris and the sulcus inferior anterior. Ingvar suggested that it be called the sulcus tonsillaris.

The lobus posterior of the vermis follows the classification of Ingvar in that with the uvula and the nodule the pyramis is included; and the division between the middle and the posterior lobes is changed from the fissura secunda between the pyramis and the uvula, to the sulcus prepyramidalis which separates the pyramis from the lobus medius posterior.

Ingvar, as already mentioned, made this change because he found that in the carnivora the prepyramidal sulcus was more prominent than the fissura secunda. This, he considered, indicated that the lobus pyramis should be grouped with the uvula and the nodule. In birds, the same classification was suggested by the arrangement of the arbor vitae. But neither of these arguments appears to be sound. In regard to the first,

Elliot Smith held that the secondary fissure was the most prominent of the posterior fissures; and while the arrangement of the arbor vitae may be suggestive, it does not seem to be reliable. In the cat, for example, the arbor vitae of the pyramis and the uvula arise from a common trunk. But in the monkey they do not, and if one is to be guided by them the pyramis distinctly belongs to the median lobe.

In the human cerebellum, the arrangement of the arbor vitae shows such an extraordinary variety that it is difficult to say what is normal. The one under consideration, which was selected on account of its clearly defined lobes and fissures, shows that the arbor vitae of each of the posterior lobes arises by a separate trunk from the central white mass, so that again the value of this factor in determining the grouping of the lobes is not supported.

In the proposed classification the pyramis is shown to belong to the posterior vermis because on stimulation it gives reactions which are exactly opposite to those obtained from the anterior vermis; e. g., when the pyramis is stimulated the anterior neck muscles contract, the head is bent forward, and there is an associated downward movement of the eyes; on the other hand, the anterior vermis on excitation produces contraction in the posterior neck muscles, the head is drawn backward, and the eyes are turned in association upward. These reactions indicate that the pyramis of the posterior vermis contains a center for the maintenance of backward balance, while the centralis of the anterior vermis regulates the mechanism of forward balance.

The value of the stimulation reactions is again shown in the uvula and nodule. The inclusion of these lobes in the posterior vermis is naturally determined by their anatomic position. But it is interesting to find that the results obtained on excitation prove that they also belong functionally to this group. For when these lobes are excited the response is in the muscles of the lips, tongue, and jaw, associated with general swallowing movements. And the axiom, that the position of the lobe is directly opposite to the reactions it gives rise to, is again demonstrated, for these lobes which occupy a posterior position in the vermis give reactions limited to the anterior part of the mouth; while the lingula, which is situated anteriorly, is associated with activities in the posterior region of the mouth, i. e., in the pharynx and the larynx. Thus, one finds that in the vermis, the uvula, nodule and lingula, i. e., the lobes forming the ventral region of the cerebellum in its relation to the brain stem, are all concerned in what is probably one of the most primitive forms of synergic movement, namely, mastication, swallowing and vocal activities. For the only reactions obtained from them refer to these regions, with occasionally some associated movements in the head and eyes. No reactions in any other parts of the body have so far been observed.

The lobus posterior of the hemisphere is composed of the lobus gracilis, the lobus biventralis, the lobus tonsillaris, the lobus paraflocculus and the flocculus.

Contrary to the views of the different authorities, the paramedian lobe of the cat is considered to be the homolog of the gracilis, biventer and tonsil of the monkey. This opinion is based partly on a careful anatomic examination of these lobes in the cat and monkey, but principally on the fact that their reactions to stimulation are exactly similar.

In the cat it was shown that the paramedian lobe was formed of three lobules, an upper, a middle and a lower. The sulcus prepyramidalis formed its dorsal boundary, the sulcus paramedianus separated it from the posterior lobe of the vermis, and the fissura secunda divided the lower lobe from the median. On stimulation, the reactions of the lobe were limited to the homolateral foreleg. The upper lobe gave responses in the shoulder, the middle lobe was related to the forearm, and the lower lobe to the foot and claws. There were no movements in any of the other limbs.

In the macacus, the gracilis, biventer and tonsil occupy the same relative positions in the hemisphere. The sulcus prepyramidalis forms the dorsal boundary, the sulcus paramedianus separates them from the posterior lobe of the vermis, and the fissura secunda divides the tonsil from the biventralis. On stimulation, the reactions of these lobes are also limited to the shoulder, forearm and hand, from above down.

Thus the similarity between the anatomic relations of the gracilis, biventer and tonsil of the monkey, and the analogy between their reactions to stimulation suggest strongly that they are the homolog of the paramedian lobe in the cat.

In the human cerebellum the lobus gracilis, biventer and tonsil offer much more in the way of comparison to the corresponding lobes in the monkey and the paramedian in the cat than is generally realized.

As in the monkey and the cat, they form the principal part of the posterior lobe of the hemisphere. The sulcus prepyramidalis, which marks the dorsal boundary, is the same, as is also the sulcus paramedianus, which separates them from the posterior vermis, the fissura secunda, which divides the tonsil from the biventralis, and the fact that a shallow sulcus indicates the division between gracilis and biventralis.

Based on these anatomic comparisons and supported by the similarity of the reactions as found in the monkey and the cat, my opinion is that the lobus gracilis, the biventer and the tonsil in man are homologous to the gracilis, biventer and the tonsil of the monkey and to the lobus paramedianus of the cat.

If the homology of these lobes is seriously considered, and it appears that it should be, it is of additional interest to note the great evolutional development that has taken place between the simple grouping of the

folia as found in the cat, and the numerous and complicated arrangement found in man. Of the three lobes the tonsil shows the greatest development. In the cat, the ventral lobule of the paramedian lobe contains but two folia. In the monkey the tonsil has already increased to four or five, while in man the tonsil contains about ninety folia. This is quite in accord with the functional activities of the part with which it is considered that this lobe is concerned, namely, the forefoot of the cat, and the hand in monkey and man. It is certainly suggestive to find that the hand which has such extraordinary powers of coordination should be represented in the cerebellum by a single lobe which has one of the most complicated formations.

The lobus paraflocculus and the flocculus show such variations in the different cerebella that a general description is difficult. In the cat and the monkey the folia of the lobes are arranged in a semicircle on the ventral surface of the hemisphere and extend from the ventral lobule of the lobus paramedianus, i. e., the tonsil, posteriorly to the lobus centralis anteriorly. They are in relation dorsally with the lobus quadratus, the lobus semilunaris superior and the lobus semilunaris inferior.

According to the reactions to stimulation, the paraflocculus in the cat may be considered to be formed of three lobules. The posterior lobule, which lies ventral to the lobus semilunaris inferior, gives reactions in the forelimb. The anterior lobule, ventral to the lobus quadratus, is in relation to the hind limb and tail. The median lobule, ventral to the semilunaris superior, has not been satisfactorily examined owing to the difficulty of reaching it, but its reactions appear to be associated with the muscles of the back.

In the monkey, only the posterior folia have been examined. These showed similar responses to those obtained in the cat, namely, reactions confined to the forelimb.

These lobes will be more fully considered in the following descriptions of the different cerebella.

PART III: DESCRIPTION OF THE CEREBELLA OF THE CAT, THE MONKEY AND MAN ACCORDING TO THE SUGGESTED CLASSIFICATION

THE CEREBELLUM OF THE CAT

If a well fixed cerebellum is allowed to dry partially and is then cut in the median line the fissures may be easily separated, and the two deepest lines of division will be found to be the primary fissure and the prepyramidal sulcus, the lobes being thus anatomically divided into anterior, middle and posterior groups, each of which has a definite and distinct functional activity.

The primary fissure lies between the lobus culminis and the lobus simplex. In the vermis, its position is perpendicular to the brain stem. Laterally it extends forward and marks the boundary, in both the vermis and the hemisphere, between the lobus anterior and the lobus medius.

The sulcus prepyramidalis is anterior to the lobus pyramis, separating it from the lobus medius. It extends across the dorsal lobule of the lobus paramedianus, and turning ventrally runs between the dorsal region of the paramedian lobe and the lobe of the semilunaris inferior. The prepyramidal sulcus thus marks the dividing line between the lobus medius and the lobus posterior in both vermis and hemispheres.

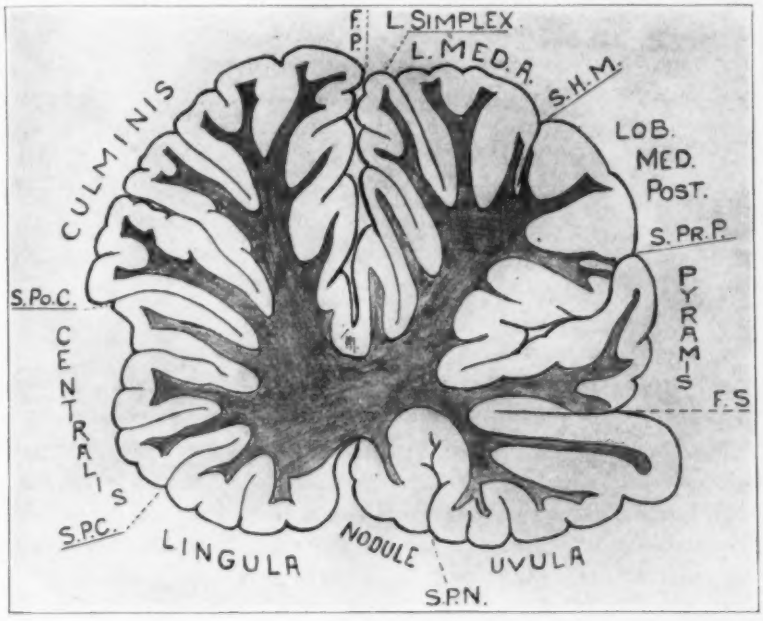


Fig. 1.—Drawing of a median sagittal section through the vermis of a cat. *F.P.* indicates the fissura prima; *F.S.*, fissura secunda; *S.P.C.*, sulcus precentralis; *S.Po.C.*, sulcus postcentralis; *S.H.M.*, sulcus horizontalis magnus; *S.Pr.P.*, sulcus prepyramidalis; *S.P.N.*, sulcus prenodularis or sulcus uvulonodularis.

The anterior lobe of the vermis is situated between the superior medullary velum and the primary fissure and contains the lingula, the centralis and the culmen. In the specimen under consideration, nine distinct fiber arms are shown running between the cortex and the medullary center. These arms are separated by three deep fissures which mark the limitations of the individual lobes.

The lobus lingulae is formed of two main lobules, each superficially divided, and has two fiber arms. Lying freely on the superior medul-

lary velum, it forms with the latter the anterior wall of the cerebellar ventricle. The sulcus precentralis marks its anterior border.

The lobus centralis occupies a median position on the anterior lobe and rests against the posterior surface of the corpora quadrigemina. The three main folia of which it is composed are connected with the central fiber mass by individual arms. As each of the main folia is superficially divided, the surface of the lobe shows six folia. It is limited ventrally by the sulcus precentralis, while dorsally the sulcus postcentralis divides it from the culmen.

The lobus culminis forms the dorsal half of the anterior lobe. It is composed of two main lobules with separate fiber arms which connect them with the central white mass. The ventral lobule shows two or three primary folia on its exposed surface and three secondary folia in the sulcus which limit it dorsally. The dorsal part of the lobe shows three lobules with separate fiber arms arising from a common trunk. The exposed cortex shows three folia each of which is subdivided. There are in addition three or four folia on its posterior surface. Though the culmen is broader than the centralis, its folia do not extend into the hemispheres, but are limited by the primary fissure which marks its posterior and lateral borders.

The middle lobe of the vermis is composed of the lobus simplex, the lobus medius anterior and the lobus medius posterior. These three lobes are really one, for in a medial sagittal section they are seen to arise from a common fiber trunk.

The lobus simplex consists of one superficial cortical folium which is continued into the hemispheres laterally and ventrally. It lies like a horseshoe around the posterior and lateral borders of the culmen, from which it is separated by the primary fissure. There are five subfolia on its anterior surface.

The lobus medius anterior is a small lobe subdivided into two. It has a common fiber arm which arises from the main trunk. In the diagram a third subdivision is indicated. It is similar in breadth and extent to the lobus simplex, and like it extends into the hemispheres laterally and ventrally under the arm of the simplex to which it is finally united. It might easily be considered as part of the simplex, but the median saggital section shows it to be distinctly separate.

The well marked transverse fissure which divides it from the S-shaped folia of the lobus medius posterior can be easily followed laterally as it passes posterior to the lobus quadratus, and then ventrally between the latter and the lobus semilunaris superior.

Though the great horizontal sulcus found in the human cerebellum and in that of the monkey has not been identified in the cat, the

prominence of this fissure in the present specimen and its anatomic relations strongly suggest that it is the homolog of the sulcus horizontalis magnus.

The lobus medius posterior in the cat, as in all carnivora, has a striking appearance. The present specimen shows it to be formed of eight folia, which are roughly arranged in the form of the letter "S" laid horizontally. Four of these folia lie on either side of the median line.

In a median section through the vermis the extent of this lobe cannot be appreciated, though the arrangement of the fiber arms in the accompanying sagittal sketch and the position of the folia in the flat projection will indicate its complexity. A horizontal section through these folia shows that there is an overlapping. And experiment has demonstrated that when the cells of the folia on the left side have been destroyed, their axons can be followed to the right to connect with the right roof nucleus, and vice versa.[14]

The great horizontal fissure limits this lobe anteriorly, and it is separated from the lobus pyramidis posteriorly by the sulcus prepyramidalis. Laterally it lies against the dorsal folia of the lobus paramedianus.

The posterior lobe of the vermis includes the lobus pyramidis, the lobus uvulae and the lobus noduli. The dorsal boundary is marked by the sulcus prepyramidalis. Ventro-anteriorly, it rests on the inferior medullary velum, while laterally it is limited by the sulcus paramedianus. The fissura secunda divides the pyramis from the uvula and the nodule. Stimulation results suggest that the pyramis alone should be considered as the posterior lobe, while the uvula and nodule with the lingula, on account of their associated reactions, should be considered as a ventral group. This question will be considered more fully when the stimulation experiments are dealt with.

The lobus pyramidalis is formed of one main lobe subdivided into three folia. Each folium shows an independent fiber arm which arises from a common trunk connecting with the central white mass. It is bounded dorsally by the sulcus prepyramidalis, while ventrally the fissura secunda divides it from the uvula. On either side is the fissura paramedianus separating it from the paramedian lobe.

The lobus uvulae is formed of one well defined lobe the surface of which is subdivided into three main folia. Each of these has a separate fiber arm arising from a common trunk. The fissura secunda marks its dorsal limit, while the sulcus uvulonodularis separates it from the nodulus. The paramedian fissure limits it laterally.

---

14. Mussen, A. T.: Experimental Investigations of the Cerebellum, Brain **50**:330, 1927.

The lobus noduli is a single lobe with a single fiber arm. It is divided into four subfolia. Lying on the posterior medullary velum, it forms with the latter the posterior wall of the cerebellar ventricle.

The Cerebellar Hemisphere.—In the cat's cerebellum, the hemisphere is formed of the middle and the posterior lobes. The anterior lobe of the vermis contributes nothing. The middle lobe includes the lobus simplex, the lobus quadratus and the lobus semilunaris superior and inferior. The posterior lobe includes the lobus paramedianus (which is here considered to be the homolog of the gracilis, biventer and tonsil, from the reactions obtained), the paraflocculus and the flocculus.

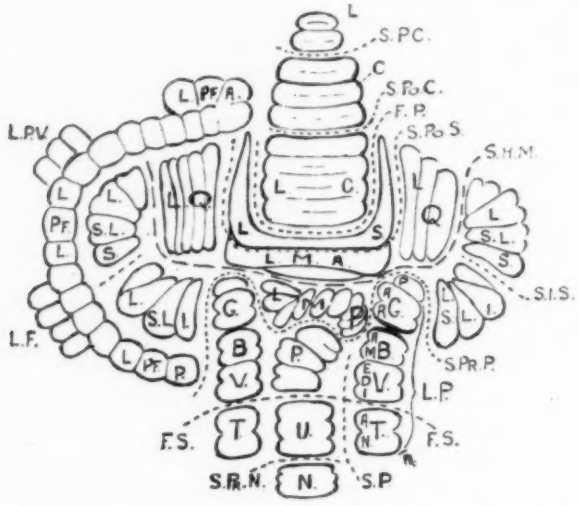


Fig. 2.—Diagrammatic presentation of the cerebellar lobes of the cat in a flat projection, to show the arrangement of the lobes, the number of the folia in each, and the fissures which divide them. The lobes are: *L.*, lingula; *C.*, centralis; *L.C.*, lobus culminis; *L.S.*, lobus simplex; *L.M.A.*, lobus medius anterior; *L.M.P.*, lobus medius posterior; *P.*, pyramis; *U.*, uvula; *N.*, nodulus; *L.Q.*, lobus quadratus; *L.S.L.S.*, lobus semilunaris superior; *L.S.L.I.*, lobus semilunaris inferior; *G.*, gracilis; *B.V.*, biventer; *T.*, tonsil. These last three represent the lobus paramedianus. *L.PF.A.*, lobus paraflocculus anterior; *L.PF.P.*, lobus paraflocculus posterior; *L.PF.L.*, lobus paraflocculus lateralis; *L.P.V.*, lobus paraflocculus ventralis; *L.F.*, lobus flocculus. The fissures are: *S.P.C.*, sulcus precentralis; *S.PO.C.*, sulcus postcentralis; *F.P.*, fissura prima; *S.PO.S.*, sulcus postsimplex; *S.H.M.*, sulcus horizontalis magnus; *S.I.S.*, sulcus intrasemilunaris; *S.PR.P.*, sulcus prepyramidalis; *S.P.*, sulcus paramedianus; *F.S.*, fissure secunda; *F.Pr.N.*, sulcus prenodularis.

The lobus simplex consists of one well developed folium which surrounds the lobus culminis laterally and posteriorly, and from which it is separated by the primary fissure. The sulcus postsimplex limits it laterally, dividing it from the lobus quadratus.

The lobus quadratus forms the main part of the anterolateral surface of the hemisphere. The present specimen shows that this lobe is composed of three well defined folia on the right and five narrow folia on the left side. Medially, it is bounded by the sulcus postsimplex, while the sulcus horizontalis magnus separates it laterally from the lobus semilunaris superior, and posteriorly from the lobus semilunaris inferior and the lobus paramedianus.

The lobus semilunaris superior is formed of four main folia which are partially subdivided into seven. It occupies the anterolateral apex of the hemisphere and lies in the form of a wedge between the lobus quadratus medially, from which it is separated by the sulcus horizontalis magnus, and the lobus semilunaris inferior, posteriorly. Ventrally, it rests on the folia of the paraflocculus.

The lobus semilunaris inferior occupies the posterolateral angle of the hemisphere. It is composed of four well developed folia which are wedged in between the lobus paramedianus medially, the lobus semilunaris superior laterally, and the lobus quadratus anteriorly. The sulcus horizontalis magnus divides it from the latter, while the fissura paramedianus marks its medial border.

The posterior lobe of the hemisphere consists of the lobus paramedianus, the paraflocculus and the flocculus.

The lobus paramedianus lies parallel to the lobes of the posterior vermis. It is composed of three main divisions which, uniting into a common stalk, project downward and forward into the ventrolateral region of the cerebellum. The dorsal division shows two folia subdivided into three; the middle division is made up of two folia subdivided into four, while the ventral consists of one main folia which is only superficially divided. These three divisions of the paramedian lobe suggest a strong anatomic comparison with the lobes of the gracilis, biventer and tonsil as found in the monkey's cerebellum and in man. This comparison is strengthened by the reactions of these lobules to stimulation, to which reference has already been made. The boundaries of this lobe are well defined. It is separated from the posterior lobe of the vermis by the sulcus paramedianus, while the sulcus prepyramidalis divides it from the middle lobe of the vermis, the lobus quadratus, and the lobus semilunaris inferior.

In the flat projection of the cerebellar lobes of the cat, the course that the prepyramidal sulcus takes may appear unusual. After passing transversely between the anterior border of the pyramis and the lobus medius posterior, it turns dorsally to swing around the upper extremity of the lobus paramedianus and then ventrally, separating this lobe from the lobus semilunaris inferior and the paraflocculus. The reason for this is that the upper and median portions of the paramedian lobe are practically united, for only a superficial sulcus indicates a division; and

as in my opinion, based on the results of stimulation, this paramedian lobe is the homolog of the lobus gracilis, biventer and tonsil which in the cerebella of both monkey and man are separated from the median lobe of the hemisphere by the sulcus prepyramidalis, so in the cat, in order to preserve a uniformity in description, this sulcus is considered to follow the course indicated.

The lobus paraflocculus and the flocculus are formed of about twenty or more folia which arise from a broad flat pedicle from the ventrolateral region of the hemisphere. Spreading out fanwise they extend from the lateral border of the paramedian lobe posteriorly, along the ventral surfaces of the lobus semilunaris inferior and superior, and the lobus quadratus to the lateral border of the lobus centralis anteriorly. Then turning ventrally and laterally over the superior cerebellar arm, they swing inward and backward over the middle cerebellar arm to take up a position ventral to the first layer.

The specimen under consideration shows twenty-eight folia. In the diagram as shown in the flat projection, these are enlarged and placed lateral to the middle lobes of the hemisphere in order to illustrate their relative positions. Of these, the eighteen lying dorsally and three ventroanteriorly may be considered to form the paraflocculus. According to Elliot Smith, the next three ventral folia form the paraflocculus ventralis, while the last four make up the flocculus. No authority is quite clear on this point, and it is difficult to make any distinction in the cat.

THE CEREBELLUM OF MACACUS RHESUS

In considering a comparison between the cerebellum of the monkey and that of the cat, it would appear at first sight that there were great differences. But a careful examination of the lobes and fissures shows how close a similarity exists. Even as to size, there is not much change. In medium sized monkeys and full grown cats the anteroposterior and perpendicular diameters are the same, while in the transverse diameter the monkey's cerebellum is only 1 cm. wider, this extra width being due to the broadening out of the middle lobe of the hemisphere.

In a well fixed cerebellum, if the fissures and sulci are opened and cleared of pia and vessels, it will be found that the primary fissure is the deepest; that it practically bisects the cerebellum, and that its position, as in the cat, is at right angles to the brain stem. The next deepest division is the sulcus prepyramidalis. These two landmarks extend from one side of the cerebellum to the other and divide both hemispheres and vermis into anterior, middle and posterior lobes, each of which has its own particular function.

The Cerebellar Vermis.—The anterior lobe, which is situated between the superior medullary velum and the primary fissure, contains the lobus lingulae, the lobus centralis and the lobus culminis. The lobus

lingulae is composed of one folium superficially divided into three, with a single fiber arm connecting it with the central white mass. It rests on the superior medullary velum, from which it lies quite free, and forms with the velum the anterior wall of the fourth ventricle. The sulcus precentralis divides it from the lobus centralis.

In comparison with that of the cat, the lingula is much smaller. It is composed of one lobule instead of two, and has one fiber arm in place of the two shown in the cerebellum of the cat.

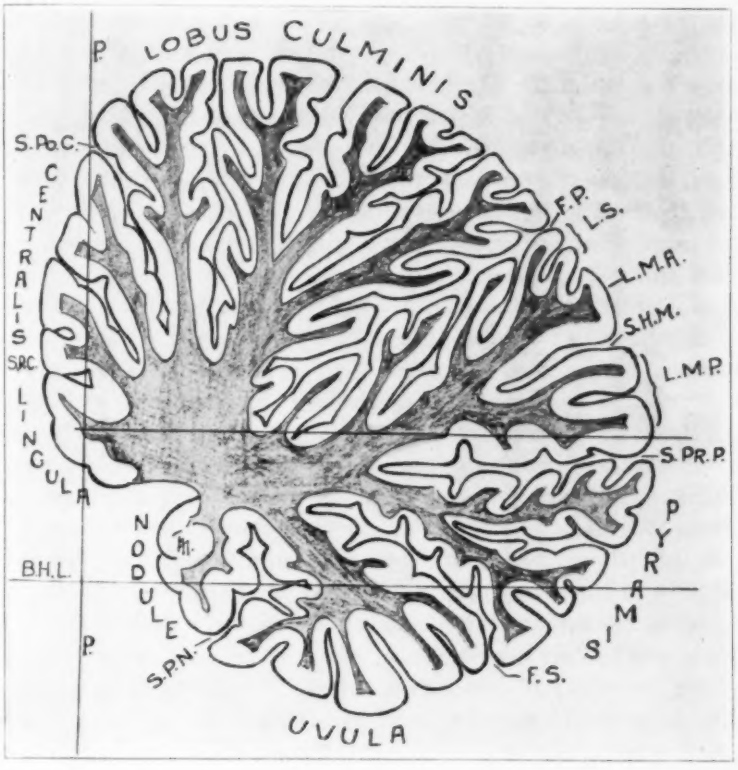


Fig. 3.—Drawing of a median sagittal section through the vermis of the monkey (Macacus rhesus). The lines *P.* and *B.H.L.* indicate the perpendicular and the basal horizontal lines and refer to the position of the cerebellum in relation to the stereotaxic instrument. *S.P.C.* indicates sulcus precentralis; *S.PO.C.*, sulcus postcentralis; *F.P.*, fissura prima; *L.S.*, lobus simplex; *L.M.A.*, lobus medius anterior; *S.H.M.*, sulcus horizontalis magnus; *L.M.P.*, lobus medius posterior; *S.PR.P.*, sulcus prepyramidalis; *F.S.*, fissura secunda; *S.P.N.*, sulcus prenodularis.

The lobus centralis occupies a median position in the anterior lobe and rests against the posterior surface of the corpora quadrigemina. It is composed of two main lobules with separate fiber arms. Each lobule

is superficially divided, so that on the surface the lobe is represented by four folia which are prolonged into the hemispheres for a short distance. It is limited ventrally by the sulcus precentralis, while dorsally the sulcus postcentralis divides it from the culmen.

The lobus culminis, the most dorsal of the anterior lobes, lies between the fissura postcentralis and the primary fissure. It is made up of four lobules which in the sagittal sketch are seen to be separated into two main divisions. The anterior, which has a separate fiber arm, is divided into three surface folia. Three extra folia are shown on its anterior border in the depth of the fissura postcentralis, and four are found in the deep fissure which limits the lobe posteriorly. The posterior or main division of the lobe is formed of three lobules, which arise from a common stalk. The first is divided into two superficial folia, the second into three, and the third into two. In addition to the seven surface folia, twenty-one other subfolia are found within the fissures of the lobe. The first two and the last superficial folia extend into the hemispheres; the middle folia are short and are limited to the vermis.

The formation of this lobe is similar to that found in the cat. In each, there are two lobules with separate fiber arms. The first lobule is narrow, with a well developed fiber arm and three surface folia. The second lobule is broad and shows three main divisions, with separate fiber connections arising from a common trunk and seven surface folia.

The lobus medius of the vermis is composed of the lobus simplex, the lobus medius anterior, and the lobus medius posterior. As in the cat these three lobes have a common fiber stalk connecting them with the central white mass, but the lobe is much smaller in comparison, principally because of the difference in the lobus medius posterior. The anterior boundary is marked by the primary fissure; the sulcus prepyramidalis limits it posteriorly, while the sulcus horizontalis magnus separates the lobus medius anterior from the lobus medius posterior.

The lobus simplex is composed of a narrow superficial folium and five well developed subfolia in the depth of the primary fissure. In the present specimen the median portion of the lobe is seen to be continued into the hemispheres, but in many cerebella the vermal portion of the lobe is covered entirely by the lobus medius anterior. The sulcus postsimplex marks its posterior border.

The lobus medius anterior is formed of two folia, which through a common fiber stem are united to the lobus simplex and the lobus medius posterior. It is bounded posteriorly by the sulcus horizontalis magnus. Laterally, it is connected with the lobus quadratus.

The lobus medius posterior consists of one, sometimes two, folia with separate fiber arms linked to the main trunk of the median lobe. Laterally, it is joined by a narrow stalk with the lobus semilunaris

superior. It is limited anteriorly by the sulcus horizontalis magnus and posteriorly by the sulcus prepyramidalis. In addition to the superficial folia, three subfolia are found within the sulcus posteriorly.

The lobus posterior includes the pyramis, the uvula and the nodule. Dorsally it is bounded by the sulcus prepyramidalis; ventro-anteriorly, it rests on the superior medullary velum and forms with the latter the posterior wall of the fourth ventricle. Laterally, the sulcus paramedianus divides it from the posterior lobe of the hemisphere. The fissura secunda, which is much more prominent than in the cat, separates these lobes into two groups: the pyramis dorsally and the uvula and nodule ventrally. In view of experimental observations, it appears reasonable to consider that the uvula, nodule and lingula, as in the cat, form a ventral group, while the pyramis alone forms the posterior lobe. For the present, the usual posterior group will be described.

The lobus pyramidis, which is the largest of the posterior group, consists of six surface folia. Dorsally, it is separated from the lobus medius posterior by the sulcus prepyramidalis; ventrally, the fissura secunda divides it from the uvula. In sagittal section the lobe is pyramid-like in form and is divided by a deep sulcus into two main divisions each of which has a single fiber arm arising from a common trunk. The cortical surfaces of the lobe within the fissures show twelve additional folia.

The lobus uvulae is the middle of the posterior lobes. It shows five surface folia which are bounded posteriorly by the fissura secunda and anteriorly by the sulcus postnodularis. Laterally, the sulcus paramedianus separates it from the ventral division of the paramedian lobe.

The lobus nodularis is the smallest of the posterior group. It is composed of three surface and two hidden folia which are supplied by a single fiber arm. The sulcus uvulonodularis separates it from the uvula. Anteriorly, it rests on the posterior medullary velum and forms the posterior wall of the cerebellar ventricle.

The Cerebellar Hemisphere.—In the cerebellum of *Macacus rhesus* the hemisphere may be said to be formed, for the sake of description, of anterior, middle and posterior lobes. But in reality it is built up principally by the great expanse of the middle lobe, which consists of the lobus simplex, lobus quadratus, the lobus semilunaris superior and inferior, and the lobus posterior, which includes the lobus gracilis, the lobus biventralis, the tonsillaris, the paraflocculus and the flocculus. The anterior lobe is represented only by the slight lateral expansion of the culmen and the alae of the lobus centralis. As in the cat, the primary fissure and the prepyramidal sulcus are taken as the lines of division.

In the lobus anterior of the hemisphere, the lingula is not represented, its folia being confined to the vermis.

The alae of the lobus centralis consist of three well defined folia which extend laterally and forward around the corpora quadrigemina posterior.

The lobus culminis sends four prolongations into the lateral lobe, the two anterior and the two posterior. These extend forward and downward to rest against the anterior extremity of the paraflocculus, and form the anterior third of the dorsal surface of the hemisphere. The primary fissure marks its posterior border.

The lobus medius of the hemisphere is composed of the lobus simplex, the lobus quadratus and the lobus semilunaris superior and

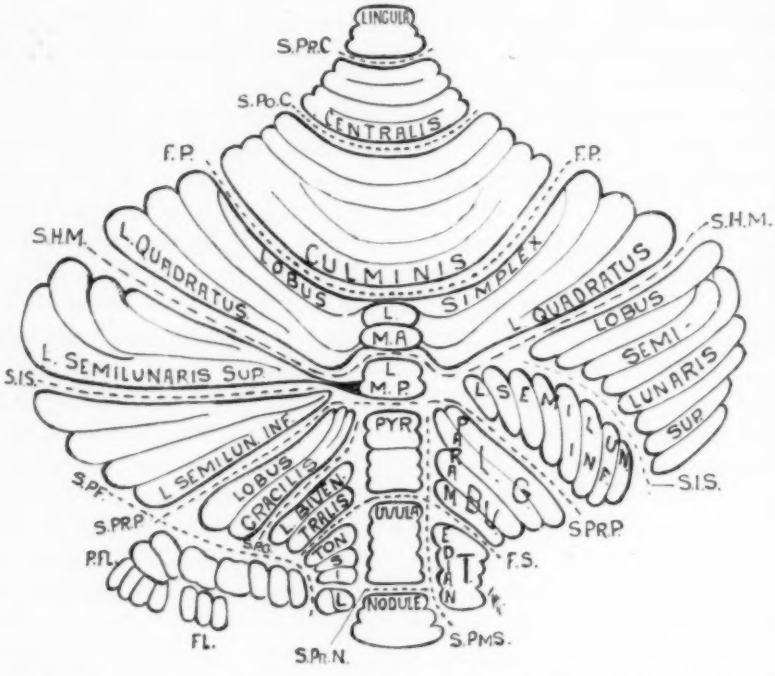


Fig. 4.—Diagrammatic presentation of the cerebellar lobes of the monkey in a flat projection to show the arrangement of the lobes, the number of folia in each and the fissures that divide them. *L.M.A.* is the lobus medius anterior; *L.M.P.*, lobus medius posterior; *PYR.*, pyramis; *P.FL.*, paraflocculus; *FL.*, flocculus; *S.PR.C.*, sulcus precentralis; *S.PO.C.*, sulcus postcentralis; *F.P.*, fissura prima; *S.H.M.*, sulcus horizontalis magnus; *S.I.S.*, sulcus intrasemilunaris; *S.PR.P.*, sulcus prepyramidalis; *S.P.G.*, sulcus postgracilis; *F.S.*, fissura secunda; *S.PMS.*, sulcus paramedianus; *S.PR.N.*, sulcus prenodularis or uvulonodularis; *S.P.F.*, sulcus paraflocculus.

inferior. It is bounded anteriorly by the primary fissure, posteriorly by the sulcus prepyramidalis, and is divided by the sulcus horizontalis magnus.

The lobus simplex consists of a single surface folium which is continuous from one hemisphere through the vermis into the other. It unites laterally with the anterior folium of the lobus quadratus from which it is only superficially separated throughout its entire extent by a shallow sulcus. In the monkey, this lobe is hardly to be considered as a separate entity. Five subfolia are found within the primary fissure which marks its anterior boundary.

The lobus quadratus consists of from three to five surface folia which unite into two as they reach the vermis. The anterior is superficially continuous with the anterior folium of the lobus medius anterior of the vermis, while the posterior has a deep association with the posterior folium of the same lobe. Anteriorly the lobe is bounded by the lobus simplex and the primary fissure. Posteriorly it is separated from the lobus semilunaris superior by the sulcus horizontalis magnus, in the depth of which three extra folia belonging to the lobe are found.

The lobus semilunaris, superior and inferior, show a greater variation than any of the other lobes of the cerebellum. In my recent experiments on stimulation, the cerebella of fourteen monkeys (*Macacus rhesus*) were carefully examined as to the composition of the lobes and many differences were observed. The most unusual change is represented on the right side of the flat projection of the cerebellar lobes (fig. 4), the left side showing what may be considered as the usual arrangement. The peculiar grouping of the folia of these lobes on the right side is of particular interest in that it closely resembles the arrangement that is found in the cat. It gives strong support for an anatomic comparison between these lobes in the cat and the monkey, which is greatly strengthened by the similarity of the reactions obtained on stimulating these lobes in both animals.

The lobus semilunaris superior, as shown on the left side of the diagram (fig. 4), is the usual arrangement. It is composed of two main folia divided by a shallow sulcus. Each of these is again subdivided in its lateral portion. The lobe is wedge-shaped. Broad laterally, it tapers off medially to a thin folium which is connected with the lobus medius posterior of the vermis. Its anterior boundary is the sulcus horizontalis magnus, while posteriorly the sulcus intrasemilunaris separates it from the inferior division of the lobe. On the anterior surface of the lobe, within the depth of the horizontal sulcus, four extra folia are found. In the usual arrangement of the lobe, there are therefore four superficial and four deep folia.

In the lobus semilunaris superior, as represented on the right side, there are also four main folia, each of which is divided. The lobe is therefore composed of eight folia, as on the left side, but here they are all found on the surface as in the cerebellum of the cat. The boundaries and relations are the same.

The lobus semilunaris inferior on the left side is formed of two main folia, each of which in its broad lateral region is divided by a median sulcus. Two fiber arms connect this lobe with the central white mass. Six extra folia are found in the sulcus intrasemilunaris and the sulcus prepyramidalis, which mark its anterior and posterior borders.

The lobus semilunaris inferior on the right side is also composed of four main folia, each of which is subdivided so that eight surface folia are shown.

The simple superficial grouping of the folia forming these lobes as shown on the right, and the fact that they are equal in number to those of the ordinarily arranged lobes as shown on the left side of the diagram is particularly interesting, in that it suggests the manner in which out of the lower simplex forms, through rearrangement, the higher forms are developed.

The lobus posterior of the hemisphere is composed of the lobus gracilis, the lobus biventralis, the lobus tonsillaris, the paraflocculus and the flocculus. Its anterior border is the sulcus prepyramidalis, which marks the division between the posterior and middle lobes. Medially, the sulcus paramedianus separates it from the posterior vermis.

The lobus gracilis is the largest of the posterior lobes. It is narrow and elongated and extends from the lobus medius posterior to the surface of the lateral region of the paraflocculus. The sulcus prepyramidalis marks its anterior border separating it from the lobus semilunaris inferior and the lobus medius posterior. It has three surface folia, and six extra folia are found within the sulcus postgracilis which limit it posteriorly.

The lobus biventralis shows two main folia separated by a shallow fissure. Within the sulcus postgracilis which bounds it anteriorly are two extra folia. Medially, it is divided from the vermis by the sulcus paramedianus and laterally, by the sulcus parafloccularis; posteriorly, the fissura secunda separates it from the tonsil.

The lobus tonsillaris consists of three main folia, the middle and the lower being superficially divided. On the left side in the specimen under consideration, the lowest folium is grooved by an almost perpendicular line, while the corresponding folium on the opposite side is unmarked. It may be that this perpendicular groove is an early indication of the torsion that the tonsil undergoes preparatory to the twisted form that is found in man.

The tonsil is bounded dorsally by the fissura secunda which separates it from the lobus biventralis. Medially lie the uvula and the nodule, with the sulcus paramedianus between. Laterally is the posterior extremity of the paraflocculus with its sulcus, and ventrally the lobe rests on the inferior cerebellar arm.

The question of these three lobes being homologous to the three divisions of the paramedian lobe in the cat is greatly strengthened by the fact that the reactions of the separate divisions in these animals are similar, both showing forelimb movements, the shoulder being represented dorsally, the forearm medially, and the wrist and the fingers ventrally.

The lobus paraflocculus is formed of eleven surface folia which are connected by five fiber arms to the central white mass. These folia are arranged fanwise under the lateral surface of the hemisphere. The posterior folium is in contact with the lateral border of the tonsil, and passing upward and forward it lies against the ventral surface of all the lobes of the hemisphere as far as the culminis. The folia then swing ventrally and laterally over the middle cerebellar arm to end anterior to the tuberculum acusticum. (In the diagram they are only represented posteriorly.)

The lobus flocculus is made up of the four folia which form the posterior extremity of the ventral layer. They lie dorsal to the tuberculum acusticum. A deep fissure separates the lobe dorsally and anteriorly from the paraflocculus.

THE CEREBELLUM OF MAN

In general appearance the human cerebellum varies greatly from that of the monkey both in size and in number of its folia, which are narrow and irregular. Yet the arrangement of the lobes and fissures in the vermis and the hemispheres is exactly similar, according to the present interpretation, to those found in both the monkey and the cat.

As in the description of these animals, the primary fissure and the prepyramidal sulcus divide the cerebellum into anterior, middle and posterior lobes.

The lobus anterior of the vermis includes the lingula, the centralis and the culmen. It rests on the superior medullary velum and is bounded posteriorly by the primary fissure.

The lobus lingulae in man is described by Schäfer and Symington as "a small tongue shaped group of four or five transverse laminae which may be said to lie upon the middle of the superior medullary velum." This is generally accepted. But when it is remembered that in the cat, the lingula shows two well developed folia with separate fiber arms connecting with the central medullary mass; that in the monkey there is one well developed lobe with a single fiber arm; that in both these animals the lingula rests on but is not attached to the velum medullare anterius, and finally that in both of these animals reactions have been observed in the pharynx and larynx when the base of the lingula has been stimulated, it does not seem reasonable to consider that the lingula in man has practically disappeared and is repre-

sented by only a few thin laminae which by their attachment produce but a thickening of the superior medullary velum. If this is the lingula, then in the specimen at hand it is represented by a slight grooving on the surface of the superior velum. It is 1 cm. wide by 1 cm. long. But it would appear more reasonable to consider that the lingula in man is represented by the first ventral lobule of the anterior lobe. In the cerebellum under consideration (fig. 5), it will be observed that the lingula arises from a single fiber trunk from which branches are given

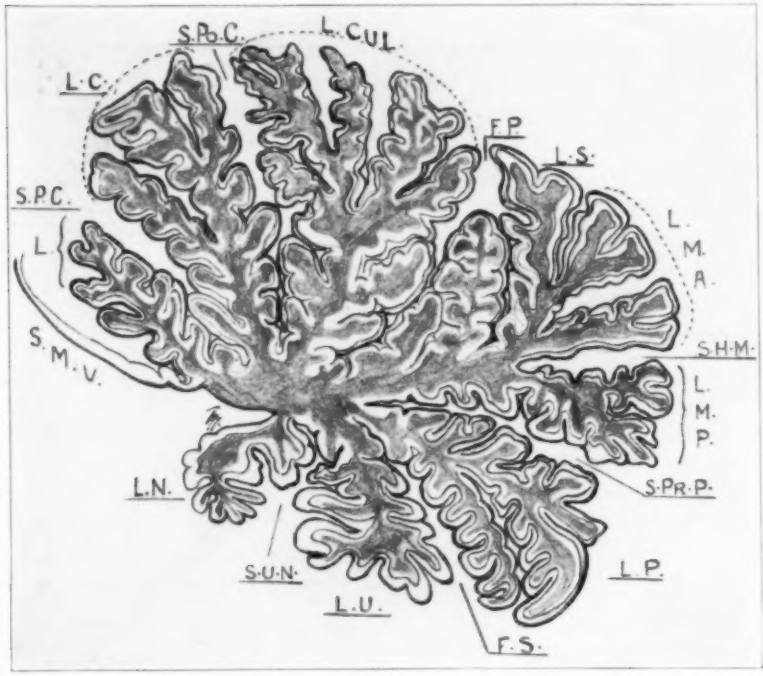


Fig. 5.—Projected drawing of a median sagittal section of a human cerebellum. *L.* indicates the lingula; *S.P.C.*, sulcus precentralis; *L.C.*, lobus centralis; *S.PO.C.*, sulcus postcentralis; *L.CUL.*, lobus culminis; *F.P.*, fissura prima; *L.S.*, lobus simplex; *L.M.A.*, lobus medius anterior; *S.H.M.*, sulcus horizontalis magnus; *L.M.P.*, lobus medius posterior; *S.PR.P.*, sulcus precentralis; *L.P.*, lobus pyramis; *F.S.*, fissura secunda; *L.U.*, lobus uvulae; *S.U.N.*, sulcus uvulonodularis; *L.N.*, lobus noduli; *S.M.V.*, superior medullary velum.

This is a rather unusual cerebellum, for it shows that each of the lobes has its own separate fiber arm connecting with the central medullary mass. Of particular interest is the fact that the lingula is represented as a separate lobe, and that the superior medullary velum shows only a slight thickening.

off to the folia on either side, and well marked prolongations extend into the hemispheres. The lobe is limited dorsally by the sulcus precentralis.

The lobus centralis also arises from a single fiber trunk which divides into three main branches and numerous secondary ones. Its anterior folia extend into the hemispheres. The posterior are short and confined to the vermis. It is limited ventrally by the sulcus precentralis and dorsally by the sulcus postcentralis.

The lobus culminis is formed about a single fiber trunk which divides into ten branches giving rise to about fifty subfolia of which six are found on the surface, the remainder being hidden within the depth of its fissures. It is separated from the middle lobe of the hemisphere by the primary fissure which marks its posterior boundary.

The lobus medius of the vermis is grouped about a single fiber trunk which gives off eight main branches around which are clustered fifty-four folia, thirteen of which are seen on the surface. It comprises the lobus simplex, the lobus medius anterior and the lobus medius posterior. The primary fissure limits it anteriorly. Posteriorly, the prepyramidal sulcus divides it from the lobus posterior.

The lobus simplex which forms the anterior portion of the median lobe has two surface folia, both of which extend into the hemispheres, and about twenty-five deep folia which arise from the common trunk of the median lobe by five separate branches, three of which are in the depth of the primary fissure, which lies between it and the lobus culminis.

The posterior limit of the lobe in both the vermis and the hemisphere is well marked by the sulcus postsimplex.

The lobus medius anterior is represented by three surface folia and one deep folium, all of which are developed about separate fiber branches which are given off from the main trunk.

Each of these folia extend into the hemisphere where they are associated with the lobus quadratus. The sulcus postsimplex bounds it anteriorly, while posteriorly it is separated from the lobus medius posterior by the sulcus horizontalis magnus.

The lobus medius posterior is developed about a single fiber branch arising from the common trunk of the median lobe, around which thirteen narrow folia are grouped, six of these being found on the surface. In the depth of the prepyramidal sulcus which limits it posteriorly a few extra folia are found. Laterally, it is connected with the lobus semilunaris superior and inferior. The sulcus horizontalis magnus limits it anteriorly.

The lobus posterior of the vermis lies between the sulcus prepyramidalis anteriorly and the posterior medullary velum. It contains the lobus pyramis, the lobus uvulae and the lobus noduli.

The lobus pyramis is the largest of the posterior lobes. It is developed about a single fiber trunk which divides into two main branches about which twenty-seven folia are grouped of which five

are on the surface. The folia are not connected superficially with the lobes of the hemisphere, but in the depth of the sulcus paramedianus which divides the posterior lobe of the vermis from the hemisphere, it is seen to be in relation with the lobus gracilis, the biventralis and the tonsil. The fissura secunda limits the lobe ventrally and the sulcus prepyramidalis marks its anterior border.

The lobus uvulae has a single fiber trunk connecting it with the central nuclei. From this numerous small branches are given off around which are developed about ten folia, four of which are on the surface. The sulcus uvulonodularis limits it ventrally. Laterally, the sulcus paramedianus divides it from the tonsil, while the fissura secunda marks its anterior border.

The lobus noduli is a small, rounded lobe which is connected to the central white mass by a single fiber arm. It lies on the posterior medullary velum, with which it forms the posterior wall of the cerebellar ventricle. It shows about six small folia, all of which are quite free from any lateral associations. Laterally lies the sulcus paramedianus, separating it from the tonsil, and the sulcus uvulonodularis limits it posteriorly.

The Cerebellar Hemisphere.—The hemisphere of the human cerebellum is also divided by the fissura prima and the sulcus prepyramidalis into anterior, middle and posterior lobes.

The lobus anterior is formed of the lateral expansions of the lingula, the centralis and the culmen. The frenulum lingulae is a thin flat projection which lies on the superior cerebellar arm. On the anterior and posterior surfaces, there are seven extra folia. It is completely covered by the lobus centralis with which it is united laterally. The sulcus precentralis marks its posterior border.

As the vermal folia of the lobus centralis extend laterally they are all united, and continue as a thin lamina which covers and extends beyond the frenulum of the lingula to which it is joined. There are about four subfolia on its anterior surface and ten posteriorly. All these converge to a single fiber arm through which they are in association with the nuclei.

The lobus culminis consists of six well defined folia which form parallel rows between the vermis and the lateral and anterior border of the hemisphere. The anterior folia are the broadest and almost completely overlap the folia of the lobus centralis. The lateral surfaces of these folia contain about sixty-eight subfolia. The lobe is limited anteriorly by the sulcus postcentralis and posteriorly by the fissura prima.

The lobus medius of the hemisphere is made up of the lobus simplex, the lobus quadratus and the lobus semilunaris superior and inferior.

The fissura prima limits it anteriorly, and the sulcus prepyramidalis marks its posterior border.

The lobus simplex in the present specimen is represented by four narrow folia which are separated by shallow diagonal sulci. Connected medially with the folia of the vermis, the lobe extends laterally to the hilus cerebelli. On its lateral surfaces sixteen extra folia are found in the depths of the fissura prima and the sulcus postsimplex which mark its anterior and posterior boundaries.

The lobus quadratus is the largest lobe of the hemisphere and forms about half of the tentorial surface. A deep sulcus divides it into a superior and an inferior lobule. The superior portion is composed

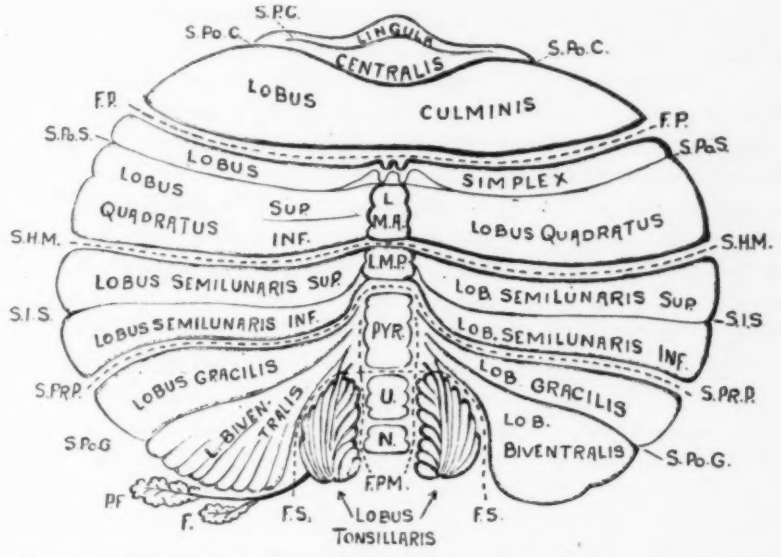


Fig. 6.—Diagrammatic presentation of the human cerebellum in flat projection, showing the arrangement of the lobes and fissures. The references are the same as in the descriptions of the monkey and the cat.

of three main folia which extend from the vermis to the hilus cerebelli. Six folia are shown on the surface, ten are found in the sulcus postsimplex and ten additional in the sulcus intraquadratus which separates it from the inferior lobule.

The lobus quadratus inferior is the broadest of the lobes of the hemisphere laterally, but rapidly tapers as it enters the hilum. Composed of eleven surface folia it gradually narrows as it nears the vermis, to the middle lobe of which it is finally attached by a thin folium. The superior and inferior surfaces are so broken up by diagonal sulci that it is almost impossible to count the number of subfolia. The posterior border is marked by the sulcus horizontalis magnus.

The lobus semilunaris superior and the lobus semilunaris inferior lie between the sulcus horizontalis magnus dorsally, and the sulcus prepyramidalis ventrally. Medially the lobes are broad, but they taper off as they dip in toward the lobus medius posterior of the vermis, to which they are attached. Laterally, only two thin folia remain. These are united, and dipping into the hilum form its ventral border. A well marked sulcus intrasemilunaris divides the lobe into two lobules. The superior contains three main folia, and the inferior two. Each of these folia is again superficially divided, with the result that ten folia are shown on the surface. In the depth of the sulci there are fifty extra subfolia.

The lobus posterior of the hemisphere lies ventral to the sulcus prepyramidalis and contains the lobus gracilis, the lobus biventralis, the lobus tonsillaris, the lobus paraflocculus and the lobus flocculus.

The lobus gracilis consists of one main lobe divided by a well marked sulcus into dorsal and ventral lobules, each of which is subdivided into three superficial folia. The lateral surfaces of the lobe show twenty extra subfolia. Ventrally, the lobe is limited by the sulcus postgracilis which separates it from the lobus biventralis; dorsally, it is bounded by the sulcus prepyramidalis, which leads directly to the anterior surface of the lobus pyramis. The lobe extends from the lateral surface of the pyramis to which it is attached, to the inferior border of the hilus cerebelli.

The lobus biventralis occupies a ventromedian position in the hemisphere. A well marked sulcus divides it into two lobules. The lateral shows three main folia and the median four. Each of these folia is superficially divided so that fourteen folia are shown on the surface, while within the sulci fifty extra subfolia are found. An interesting arrangement of these deep folia is to be observed in the depth of the fissura secunda which separates the lobe from the tonsil. On this inner surface of the lobus biventralis, the folia run forward and slightly upward in parallel rows. If the fissure is widely opened, it will be observed that some of the folia which at their central attachment are joined to the biventralis are found to be associated peripherally with the tonsil. The connection between these two lobes is obviously very close. The lobe may be described as arising from a thin lamina which is attached to the central white mass and the lateral border of the pyramis. It extends, broadening out rapidly as folia are continually added, to the ventromedian surface of the hemisphere where it rests on the paraflocculus. In its development, it completely surrounds the ventral border of the tonsil.

The lobus tonsillaris is a small circumscribed group of folia which occupies the ventromedian region of the hemisphere. It is deeply embedded in the lobus biventralis posteriorly and ventrally, while dor-

sally it is overlapped by the posterior lobe of the vermis. Anteriorly, it rests on the posterior medullary velum, with which it forms the lateral part of the posterior wall of the fourth ventricle. The fissura secunda separates the lobe from the biventralis, and the sulcus paramedianus divides it from the uvula and the nodule.

The median surface of the tonsil is marked by a deep horizontal sulcus which is continuous with the hilus cerebelli. The lobe is thus divided into a dorsal half and a ventral half. The dorsal portion which is formed of three lobules shows nine superficial folia which are arranged in parallel rows sloping diagonally forward. The ventral portion, which is composed of four lobules, shows seven superficial folia which are arranged horizontally. The lateral surface, which rests against the biventralis, contains eight surface folia. In the depth of the various fissures there are in addition about sixty-five subfolia, so that in all the tonsil contains about ninety folia. All the surface folia converge into the fossa axialis.

If the tonsil is well separated from the biventralis, it will be seen that its broad fiber trunk joins with that of the biventralis, the two being connected with the central white substance lateral to the pyramis. In the depth of the fissura secunda further evidence of the close association of these lobes is to be found, for several folia which arise in the biventralis enter into the formation of the tonsil. Thus, the gross anatomic appearance suggests that these two lobes are closely associated, which adds strength to the view that they are related functionally (as is indicated by their reactions to stimulation).

But the question of the status of the tonsil is still being debated. Ingvar [15] favored the view that it is the homolog of the lobus paramedianus. Bolk [3] considered it the equivalent of the paraflocculus; while Tilney and Riley [16] claimed that it is the hemispheral expansion of the uvula. Riley,[17] identified it with the paraflocculus.

This difference of opinion indicates clearly that it has been impossible to settle this dispute on either embryologic or anatomic grounds. It seems justifiable, therefore, to consider the reactions of these lobes in the different cerebella, and the suggestions arising from them.

It has already been shown that the paramedian lobe in the cat, which consists of three lobules, gives reactions in the shoulder, forearm and paw. As the gracilis, biventer and tonsil in the monkey show similar movements, it seems logical to consider that the gracilis, biventer and tonsil in man are homologous. According to this, it is impossible to believe that the tonsil alone is the homolog of the whole paramedian

15. Ingvar, Sven (footnote 6, p. 369).

16. Tilney and Riley (footnote 7, p. 438).

17. Riley, H. A.: The Mammalian Cerebellum, Arch. Neurol. & Psychiat. **30:** 1033 (Nov.) 1928, fig. 41.

lobe, but it is possible to consider that it is the homolog of the ventral lobule. The same argument will show that the tonsil cannot be considered as the equivalent of the paraflocculus, for the reactions of the latter are associated with movements in the hind limb, back and forelimb. But a close association apparently exists between the tonsil and the posterior folia of the paraflocculus, which are contiguous, for the reactions in each are similar.

Against the possibility of the tonsil being the hemispheral expansion of the uvula is the fact that its anatomic associations with the biventralis are obvious. For these lobes are not only connected in the depth of the fissura secunda, which separates them, but the gracilis, biventer and tonsil are all joined medially. In addition, these three lobes are united functionally as is indicated by their reactions, while the responses of the uvula are entirely different. On the other hand, the uvula and the nodule which show reactions related to mastication are flanked on either side by the tonsils, representing the movements of the hands. An interesting functional relationship is thus indicated.

The flocculus and the paraflocculus arise from the thickened lateral wall of the inferior medullary velum. The pedicle of the flocculus extends forward behind the recess of the fourth ventricle. Here it expands into the small, flat, irregular lobule which constitutes the flocculus. It is composed of a few short diverging laminae which lie between the biventral lobe and the middle peduncle of the cerebellum.

The paraflocculus is represented by small portions of laminated gray matter arising from the stalk of the flocculus. In man this is rudimentary, in rabbits it is larger than the flocculus, and projects into a well marked fossa in the petrous part of the temporal bone, and in many mammals, e.g., the swordfish, it is the most prominent lobe of the cerebellum.

Tilney and Riley support Schäfer and Symington in the opinion that the flocculus, paraflocculus and the inferior medullary velum are the lateral expansions of the lobus noduli of the vermis. While this may be correct embryologically, it suggests a functional relationship that is challenged by the results of some recent experiments on the rabbit. In several of these animals the paraflocculus was destroyed,[18] without injury to the dentate nucleus. In the Marchi stained sections, an obvious tract of degeneration was found to pass directly into the superior cerebellar arm and on to the red nucleus. This does not tally with the foregoing view; neither do the facts that the nodulus on stimulation gives reactions in the lips and tongue, while ablation of the paraflocculus results in the loss of the righting reflex on the side of the lesion.

---

18. Mussen, A. T. (footnote 14, p. 345).

COMMENTS

In the preceding discussion of the proposed classification of the cerebellar lobes and fissures, reference has been freely made to my stimulation experiments. Though these have been reported several times during the past three years, only the preliminary reactions have so far been published.[19]

It must be remembered that in my experiments an insulated double electrode was employed, and that the stimulations were in a sense subcortical, i. e., below the surface but still within the cortex. The electrode

TABLE 11.—*A General Classification of the Cerebellar Lobes Based on Their Electrical Reactions, and Applicable to the Cat, Monkey and Man*

Reactions	Vermis		Hemisphere		Reactions
Larynx-pharynx	Lingula		Lingula		
Neck muscles, posterior Head drawn back Eyes turned up	Centralis	Lobus anterior	Centralis		Neck muscles Indefinite shoulder movements
	Culmen		Culmen		
	Fissura prima				
	Simplex		Simplex		
Neck muscles Indefinite movements of shoulder, eyes	Medius ant.	Lobus medius	Quadratus		Neck muscles, posterolateral
Neck muscles Head and eyes to side stimulated	Medius post.		Semilunaris sup.		Neck muscles, lateral
			Semilunaris inf.		Neck muscles, anterolat.
	Sulcus prepyramidalis				
Anterior Neck muscles Head and eyes down	Pyramis		Gracilis	Lobus paramedianus	Shoulder
			Biventer		Upper leg
Lips, tongue, jaw, swallowing movements	Uvula	Lobus posterior	Tonsil		Foreleg, paw, claws
	Nodule		Paraflocculus		
			Anterior		Hind limb (tail)
			Median		Back ?
			Posterior		Forelimb
			Flocculus		Stimulation gives indefinite eye movement
					Destruction results in loss of righting reflex

was made of fine iridioplatinum wires, insulated in a double-barreled glass tube, the diameter of which was 1 mm. In my opinion, it was entirely due to this method of investigation that the localization of the reactions was possible. According to this view, the majority of the surface stimulations are unreliable.

Since then many more investigations have been performed which have clearly demonstrated the remarkable similarity in the reactions of homologous lobes in the different cerebella. And it is on the final results of these experiments that the possibility is based of having one

19. Mussen, A. T. (footnote 14, p. 346).

classification that would be applicable to the usual experimental animals, the cat and the monkey, as well as to man.

Attention has also been drawn to the importance of these reactions in determining the grouping of the lobes. For as the position of a lobe is opposite to the reactions it gives rise to, the group to which a lobe should belong is indicated by the character of the muscular responses obtained on stimulation. In table 11, showing the cerebellar lobes and their reactions, this axiom is clearly demonstrated.

In the vermis it will be observed that the anterior lobes give responses in the posterior neck muscles, while the pyramis of the posterior group is in relation with the anterior neck muscles. The lobus medius, which has a more complicated anatomic arrangement, still in a sense maintains a position opposite to its reactions, for when the left half of the lobe is excited the response in the head and eyes is produced through its associations with the opposite roof nucleus. The ventral lobes of the vermis show similar relations. The uvula and the nodule situated posteriorly are associated with the lips and tongue, while the lingula anteriorly is related to the larynx and pharynx.[19]

The lobes of the hemispheres are correspondingly arranged. The lobus quadratus and the simplex, which occupy an anterolateral position in the median lobe, control the muscles in the posterolateral region of the neck. The lobus semilunaris inferior which is situated posterolaterally is associated with the anterolateral neck muscles, while the lobus semilunaris superior which lies between serves the muscles of the lateral region of the neck. In the posterior lobe, the forelimb is controlled by the lobus paramedianus and the posterior lobule of the paraflocculus; the hind limb, by the anterior lobule of the paraflocculus; the middle lobule of this lobe being in relation with the movements of the back.

These reactions were shown to be of particular value in regard to the grouping of the lobus pyramis and the lobus semilunaris inferior, the position of both being under dispute.

The lobus pyramis is usually classified as belonging to the median lobe of the vermis. Recently it has been considered by Ingvar, on embryologic grounds, to belong to the posterior vermis. According to its stimulation reactions, the lobe is shown to be definitely related to the posterior group.

The lobus semilunaris inferior, which is situated on the boundary between the median and the posterior lobes of the hemisphere, is sometimes grouped with the median lobe and sometimes with the posterior. On stimulation a definite answer is obtained, for the lobe gives responses in the anterolateral neck muscles. And as the lobus semilunaris superior, the lobus quadratus and the lobus simplex are also related to the activities of the lateral neck muscles, the semilunaris

inferior clearly belongs to this group, rather than to the posterior as Ingvar suggests, the reactions of which are associated with the limbs and back.

The stimulation reactions bring to light another important cerebellar axiom, namely, that lobes which are closely associated anatomically are functionally related. And this is true not only in regard to the postural reflex activities constantly in play in the maintenance of normal balance, but also to the reflex activities of mastication and swallowing, as well as to the associated synergic movements found in the use of the forelimbs, particularly the paws or hands, in feeding.

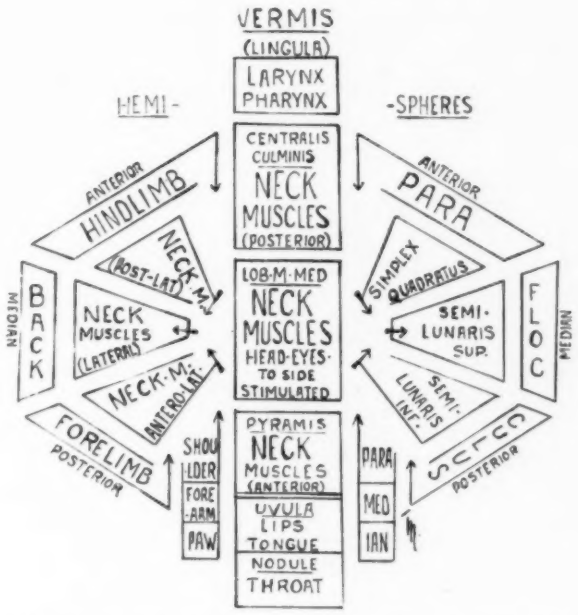


Fig. 7.—Diagram of the cerebellum to illustrate the grouping of the lobes according to their reactions to stimulation. It will be observed that with the exception of the ventral lobes of the vermis—the uvula, nodule and the lingula—the paramedian lobe and the paraflocculus, all the remaining lobes are related through their activities to different groups of the muscles of the neck.

Figure 7, a diagrammatic representation of the various lobes of the cerebellum of the cat, will help to illustrate these points.

The posterior vermis has been referred to as the center that controls backward balance. And as the uvula and the nodule are excluded, for their reactions are concerned with mastication and swallowing, the reference is limited to the pyramis alone. This means, then, that the normal function of the pyramis is to prevent any tendency to fall backward; but if the pyramis is injured, then through its inactivity it pro-

motes a tendency to fall backward. Though this statement may appear contradictory, the explanation is clear.

In health, forward and backward balance are maintained through the coordination of the anterior and posterior neck muscles. If there is a tendency to fall backward, the lobus pyramis acts, the anterior neck muscles are contracted and the head is thrown forward; then through the action of the dorsal lobules of the paramedian lobe the arms are stretched out in an effort to maintain the balance. Thus, in this reflex response, the pyramis with the adjacent paramedian lobes act together. But when the pyramis is injured, then the opposite actions become dominant. As the anterior neck muscles are no longer under the control of the pyramis, the posterior neck muscles influenced by the unopposed activity of the anterior vermis contract too strongly, and the head is pulled too far backward. Then to overcome the tendency to fall, the associated activities of the adjacent anterior lobules of the paraflocculus are brought into action, and the hind limbs are flexed in an attempt to regain equilibrium.

Between the middle lobe of the vermis and the middle lobes of the hemispheres, there is a similar coordination. It had been shown that when the lobus medius of the vermis is stimulated, the head turns toward the side excited through the action of the opposite sternomastoid muscle, and associated with this reaction is a conjugate deviation of the eyes. Further lateral movement depends on whatever influence predominates in the lobes of the hemisphere. If the movement is associated with the anterolateral region (the lobus simplex and the lobus quadratus), the head will be turned laterally and flexed posteriorly. If the relation is with the lateral region (the lobus semilunaris superior), the head will be bent toward the shoulder, while if the cooperation is with the posterolateral region (the semilunaris inferior), the head will be rotated laterally and bent forward.

In figure 7, another important point is demonstrated, namely, that all of the central lobes of the cerebellum in both vermis and hemispheres are concerned with the activities of the muscles of the neck. In fact, with the exception of the ventral lobes of the vermis—the uvula, nodule and lingula—and the paramedian lobe with the paraflocculus of the hemisphere, all the remaining lobes are related through their reactions to definited groups of muscles in the neck. This means that practically the whole of the cerebellum that can be easily exposed is in association with various groups of neck muscles.

The point of this observation is that in most stimulation experiments the head is supported in some form of a holder that prevents its movement. Consequently, when the muscles of the neck contract, owing to stimulation of the different lobes of the cerebellum, as the head is fixed the reactions are transferred to the shoulder girdle, and the characteristic

response is elevation of the shoulder. This is probably the explanation of why so many investigators have concluded that the cerebellar cortex contained no localized areas, for it appeared that wherever the cortex was stimulated the only response was elevation of the shoulder. But with the steriotaxic instrument the head is movable, so that when the different lobes are stimulated and special groups of muscles in the neck respond, the various movements of the head can be readily observed.

Another point of interest suggested by the relationship of the central lobes of the cerebellum to the activities of the different groups of muscles in the neck is the possible effect that this may have on the interpretation of the nature of the "righting reflexes."

Magnus has drawn attention to the extraordinary influence which the various positions of the head have on the righting reflexes,[20] and has claimed that the center regulating these activities is situated in the red nucleus. This view has already been questioned,[21] and Lovatt Evans,[22] in his review of these reflexes, considered that the center must be in the cervical cord, for when the posterior roots are cut the reflexes are lost.

The explanation of the righting reflexes is not clear. It is, in fact, doubtful whether at the present time they can be correctly interpreted. It is only desired to call attention here to the possibility that the cerebellum itself is well equipped for this purpose, and may indeed be the seat of these complicated reactions. For though it has been stated by Magnus and de Kleijn that the removal of the cerebellum does not interfere with the functioning of the postural reflexes, the fact that the righting reflex is lost in the rabbit when the paraflocculus is destroyed [18] is strong evidence that the cerebellum is not to be overlooked.

It will doubtless be asked what proof is there to support the view that the localized responses to stimulation represent the functional activity of the various lobes? As this question will be fully considered in a paper on the stimulation experiments, which is to appear shortly, it will be only briefly discussed here to show that the conclusions expressed are not without foundation. Strangely enough, the most important confirmations of my results are found in the earliest and the latest experiments, and not, as one would expect, among the many stimulation investigations and localized operations of recent years.

Flourens and Renzi [23] in 1864 were the first to show that lesions of the anterior part of the middle lobe, i. e., the vermis, caused the animal

20. Magnus, R.: Korperstellung, Berlin, Julius Springer, 1924.

21. Mussen, A. T.: The Red Nucleus, Tr. Am. Neurol. A., 1925.

22. Evans, C. L.: Recent Advances in Physiology, University College, London, Arnold, 1926.

23. Flourens and Renzi: Annali universali di medicina, 1864, vol. 187.

to fall forward; while a lesion of the posterior vermis produced a tendency to fall backward. This agrees exactly with my observations.

About fifteen years later, Ferrier [13] confirmed these by stimulation experiments. He also reported that when the posterior vermis was excited the head and eyes turned toward the side under examination. (As the classification of the lobes at this time was not definite, it is considered that the lobe in the posterior vermis referred to was the lobus medius posterior.) It is remarkable that these observation have only been corroborated after a lapse of sixty-five years.

Other investigators by the stimulation method include Hitzig, Prevost, Bárány and Hoshino, Kroll, Sherrington, Versilov, Prus, Bechterew, Rothmann, Dusser de Berrenne, Horsley and Clarke, and Miller. As the reports of these authors will be discussed in a following paper, it must suffice to mention here that though reactions in the head and eyes, fore and hind limbs, were frequently observed, they were not definitely localized.

Of all the investigations, the stimulation experiments of Horsley and Clarke [24] have been perhaps the most influential in the formation of the generally accepted opinion that the cerebellar cortex was not excitable.

While it is true that they worked with the steriotaxic instrument, and it was my privilege to be with them for one year at this time, neither charts nor diagrams were employed. It was consequently impossible to know after the needle had been inserted into the cerebellum, where the point was or which lobe was being stimulated. With them it was more a question of regions than of lobes, their particular interest being with the cerebellar nuclei. Nevertheless, they did report movements in the head and eyes, fore and hind limbs, though most of these were obtained in the region of the nuclei, as is shown in the photographs in Clarke's posthumous article.[25] And a careful review of their papers fails to show evidence that the cortex itself received any particular attention. In some of their notes the remark is found: "in this animal we did not waste time over the cortex." But in spite of the general belief that they considered the cerebellar cortex to be inexcitable, their final conclusion was that it did respond to the faradic stimulus, though when contrasted with the cerebral cortex it was, comparatively speaking, inexcitable.

The investigation of function by localized lesions has been generally unsatisfactory. In Horsley and Clarke's experiments,[4] the areas

24. Horsley, V., and Clarke, R. H.: The Structure and Function of the Cerebellum Examined by a New Method, Brain **31**:45, 1908.

25. Clarke, R. H.: Stimulation of the Cerebellum, Brain **50**:383 (pt. 4) 1927.

involved are always much too extensive. The destruction covers too many lobes and extends too deeply to obtain localized disturbances. The same comment applies to most of the other researches by this method.

There are nevertheless a few experimental lesions which, being circumscribed, have given definitely localized reactions.

The experiments of Flourens and Renzi already mentioned were satisfactory. Their lesions were small and well localized, and the loss of function was limited.

Another interesting research is that reported by Lauretta Bender [26] on the lobus lingula. The approach was through the fourth ventricle, and a small area in the base of the lingula was destroyed. The results showed definite motor disturbances in the vocal cords. This supports my observations by stimulation in which the larynx and the pharynx were affected, as evidenced by the production of swallowing movements —contraction of the pharynx and raising of the larynx—and in one instance a high-pitched cry.

Recently, the following experiment was performed to check the relations between the reactions to stimulation and the effect of a lesion.[27]

It has been mentioned that the dorsal folium of the lobus paramedianus responds on stimulation by reactions in the shoulder. If a stronger current is employed, the foreleg is also involved. This lobe on the left side was exposed and the middle folium of the dorsal lobule was stimulated, the usual response in the shoulder being obtained. The spherotome [28] was then inserted into the same folium, and a lesion 5 mm. in circumference was made at a depth of 2 mm. below the surface of the cortex. The following day an interesting and localized incoordination was observed. When the animal walked the left foreleg was thrown too quickly forward and too high, almost parallel to the floor. It was then brought suddenly down. After persisting for twenty-four hours, the incoordination gradually disappeared. The movements in the other legs were quite normal. This observation agrees entirely with the results of Rothmann,[29] Thomas and Durupt,[30] for they emphasized the fact that destruction of the cerebellar cortex does not produce paralysis but does give rise to incoordination.

---

26. Bender, Lauretta: The Cerebellar Control of the Vocal Cords, Iowa State Psychopathic Hospital, Iowa City, 1928.

27. Mussen, A. T.: Lesion of the Paramedian Lobe, to be published.

28. A spherotome is a needle-like instrument containing a blade which can be projected after insertion. (Clarke, B.: Investigation of the Central Nervous System, Baltimore, The Lord Baltimore Press.)

29. Rothmann, M.: The Symptoms of Cerebellar Disease and Their Significance, Seventeenth International Congress of Medicine, London, Tr. Sect. 11, 1912, pt. 1, p. 59.

30. Thomas, André; and Durupt, A.: Localisations cérébelleuses, Paris, 1914.

This experiment indicates that it will be possible to check the function of the lobes by small localized lesions and to compare the results obtained with the reactions to stimulation. If the opportunity offers, it is my intention to carry out this research during the following year.

Further evidence in support of my claim that the electrical reactions of the cerebellar lobes represent their physiologic function is to be found in the associations that exist between some particular synergic activity and a specially developed lobe. This fact has been repeatedly impressed on me in my numerous experiments on the cat. Every one is familiar with the peculiar S-shaped arrangement of folia found in the posterior vermis. These folia, which form the lobus medius posterior, are arranged horizontally there being usually four or five on either side of the median line.

When the reactions of this lobe to stimulation showed that the folia on the left side turned the head and eyes to the left, and the folia on the right side turned the head and eyes to the right, the natural conclusion was that the function of this lobe was concerned with the conjugate movements of the head and eyes to one side or the other; and conversely, that the special development of this lobe indicated unusual activity in the head and eye movements. A little investigation showed that this lobe was particularly prominent in the carnivora, which depend for their existence on a highly developed coordination between the movements of the head and eyes and the jaws.

The lobus medius posterior probably reaches its highest development in the tiger, and while it varies considerably in the different groups, it appears to become gradually less prominent in the domestic animals. In the cat, a considerable variation is found. Usually the lobe is represented by a well developed S-shaped formation. But sometimes there is only a slight irregularity in the folia of the vermis. This suggests that the character of the lobe is gradually changing, possibly owing to the fact that the cat has been more or less domesticated for about seventeen centuries. An interesting fact in this connection is that some cats are marvelously quick in catching mice while others are quite indifferent.

Though the association between the coordinated activity of the head and eyes and the lobus medius posterior in the cat has not been proved, it is nevertheless possible to confirm this relationship by a comparison of similar activities with the cerebellar development as found in other animals.

In an extraordinarily interesting paper by Riley[31] on the mammalian cerebellum, which is based on a comparison of the arbor vitae and the folial pattern, the author remarked: "It should be a matter of

31. Riley, H. A.: The Mammalian Cerebellum, Arch. Neurol. & Psychiat. **20**:895 (Nov.) 1928.

considerable probability that the patterns evidenced in the disposition of the folial chain should have some direct relationship to the physical characteristics of the animal to which the particular cerebellum belongs." And then after a description of the examinations of the cerebellums of a wide variety of mammals, which include *Marsupialia, Edentata, Ungulata, Cetacea, Carnivora, Pinnipedia, Rodentia, Chiroptera* and the primates, the opinion is expressed that "functional localization in the cerebellum on the basis of this study is impossible."

As this conclusion is directly opposed to the results of my stimulation experiments, I feel compelled to question it, particularly as it is possible to demonstrate from the examples given in Riley's paper that such a view is not justified.

From the description of the various specimens examined and the accompanying illustrations, it is possible to compare the special characteristics of each mammal with the lobes of the cerebellum, for the vermis is represented in sagittal section and the hemisphere in a flat projection.

In the group of mammals examined there are several in which the movements of the head and eyes are particularly active, and it will be shown that when such activity is present it is always accompanied by a special development of the lobus medius posterior.

It has been stated that my stimulation experiments have shown that the middle lobe of the vermis—lobus medius posterior—is concerned with the coordinated movements of the head and eyes toward one side or the other. Now, if it is true that these reactions to stimulation represent the functional activity of the lobe one would expect to find that the middle lobe of the vermis would be particularly prominent in those animals whose existence depends on a high degree of efficiency of this particular mechanism; and conversely that the lobe would be poorly developed in those animals in which the head and eye movements were sluggish and unimportant.

The reindeer might be cited as a type of the first. Its ability for attack and defense lies in the accurate coordination of the head and eyes with the antlers, and in this animal the middle lobe of the vermis shows a high degree of development, particularly in its posterior region, which is rich in foliation and in the number of its arbor vitae.

On the other hand, the sloth shows exactly the opposite. This animal is sluggish, almost blind and practically deaf. Most of its existence is spent hanging from the limb of a tree. In feeding, the forelimbs are used to drag leaves and twigs awkwardly to its mouth. In this case the head and eye movements are obviously unimportant, and one finds that the middle lobe of the vermis is simply organized.

Following the same argument of special development for the maintenance of existence, one finds another example in the swordfish which

derives its remarkable power of attack from its tail. In this mammal, there is an extraordinary development of the paraflocculus, particularly in its anterior region; and the stimulation reactions show that the cerebellar center for coordinated movements of the hind limbs and tail lies in the anterior lobule of the paraflocculus.

A converse example is found in the beaver. Though this animal has a well developed and useful tail, its function is really limited, and the paraflocculus is found to consist of a few small folia.

Other instances of the association between special function and well organized cerebellar lobes are found in those mammals in which the movements of the lips and tongue are markedly active.

The camel, reindeer, giraffe and the manatee may be taken as outstanding types in which the lips and tongue are actively prehensile and mobile. In each instance examination of the cerebellum shows that the uvula and the nodule are prominent. And it is in these lobes that the reactions to stimulation have shown that the movements of the lips and tongue are located.

On the other hand, the dolphin, the swordfish and the sloth have short inactive tongues, and in these the uvula and the nodule are poorly developed.

From these, and many other examples that might be cited, it is clear that there are strong grounds for the belief that special activities in the animal are represented by some particular development of the cerebellar lobes, and that the electrical reactions of the individual lobes are to be considered as representing in a general way their functional activities.

It may be of interest to recall that when reports were published by Hughlings Jackson,[32] Ferrier [13] and others that the cerebral cortex contained motor centers the condemnation was general. It was considered that if any movement did occur it could only be through the spread of the current to the spinal and bulbar nuclei. Brown-Séquard [33] and Dupuy [34] were particularly active in their opposition. And though the stimulation of the cerebral cortex is a comparatively simple matter, open to any investigator with a faradic battery, it was nevertheless several years before the facts were generally accepted, and then only when the evidence from all sides had proved them to be correct.

Unfortunately, the stimulation of the cerebellar cortex is an entirely different matter. It is my belief that localized reactions can be satisfactorily obtained only by the use of the steriotaxic instrument. But

32. Jackson, Hughlings: Evolution and Dissolution of the Nervous System, Brit. M. J., 1884.

33. Brown-Séquard: Entre-croisements des conducteurs servant aux mouvements volontaires, Arch. de physiol. norm. et path. **1**:218, 1889.

34. Dupuy, E.: The Rolandic Area of the Cortex, Brain **15**:190, 1892.

even with this instrument a great deal of time is required, and as there are probably only three instruments in existence, the outlook for the confirmation of my results is not good.

Nevertheless, there are indications of a changing attitude.

Tilney and Riley [35] stated that "the evidence derived from stimulation of the cerebellar cortex seems to be conclusive, not only as to its experimental excitability but also with reference to the presence of localized functional areas within it."

Mills and Weisenburg [36] have claimed "that the fundamental function of the cerebellum is synergia." This is defined as "the power or faculty by which movements more or less complicated but functionally definite are associated in special acts." This view is entirely in accord with my stimulation results. In figure 7 it is clearly shown that the anatomic arrangement of the lobes is such that this synergic function may be most economically exercised.

Probably one of the best examples of this grouping of the lobes that are functionally associated is that which relates to what is possibly the most primitive form of synergic activity, namely, the function of coordinating the movements of the lips, tongue and throat with the activities of the forelimbs in the act of feeding, which may be observed in any litter of kittens. The lobes which have this power or faculty by which movements more or less complicated but functionally definite are associated in special acts are the uvula, the nodule and the lingula, which are grouped together on the ventral surface of the vermis, with the paramedian lobes on either side.

In an interesting paper on "The Cerebellum," Dr. Charles K. Mills wrote: "I do not believe it is correct to infer as Horsley and Clarke have done, that the large volume of purely cerebellar tissue known as the folia has no distinct function except that of receptors." And again "I am as firm a believer in cerebellar localization as I am in the localization of centres and areas in the cerebrum." [37]

Such opinions encourage me in the belief that the views expressed in this paper will be favorably received. It is presented with the hope that by giving a clearer idea of the grouping of the lobes of the cerebellum, founded on their functional activities as shown by stimulation, the early symptoms of cerebellar disease may be more readily appreciated.

---

35. Tilney and Riley (footnote 7, p. 465).

36. Mills, C. K., and Weisenburg, T. H.: Cerebellar Symptoms and Cerebellar Localization, J. A. M. A. **63**:1813 (Nov. 21) 1914.

37. Mills, C. K.: The Cerebellum, Arch. Neurol. & Psychiat. **20**:235 (Aug.) 1928.

CORTICAL ANOMALIES, VENTRICULAR HETEROTOPIAS AND OCCLUSION OF THE AQUEDUCT OF SYLVIUS*

JAMES W. KERNOHAN, M.B., CH.B.
ROCHESTER, MINN.

True heterotopia of the brain is not common, although a considerable number of cases is reported in the German literature, but few in French, English or American literature. Heterotopias vary much in size, site and number, and when present they usually are multiple. Tüngel [1] found heterotopias of gray substance in the wall of the lateral ventricle, whereas Meschede [2] found as many as eighty heterotopic nodules in the walls of the lateral ventricles. Virchow [3] described heterotopic nodules in a brain, saying that they appeared as if a gyrus was placed in the white substance. Ermann [4] found about thirty such nodules and Hoffmann [5] saw ganglion cells, with fatty degeneration, in some heterotopic islands. Otto [6] had three cases with nodules in the ventricular walls, whereas Wicke [7] described a case of heterotopia in the centrum semiovale. Matell [8] described a case of massive heterotopia underneath the cortex in the white matter, and in which the cortex was separated from the heterotopic portion by a narrow band of myelinated fibers belonging to the association system. There were bridges of fibers

* Submitted for publication, Oct. 7, 1929.

* From the Section on Pathologic Anatomy, the Mayo Clinic.

* Work done in the Anatomic Laboratory of Prof. A. Jakob, Staatskrankenanstalt-Friedrichsberg, Hamburg, Germany.

* Read before the Section on Nervous and Mental Diseases at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 12, 1929.

1. Tüngel, C.: Ein Fall von Neubildung grauer Hirnsubstanz, Virchows Arch. f. path. Anat. **16**:166, 1859.

2. Meschede, Franz: Ein neuer Fall von abnormer Einlagerung grauer Hirnsubstanz innerhalb der Medullarsubstanz des grossen Gehirns, Virchows Arch. f. path. Anat. **37**:567, 1866.

3. Virchow, Rudolf: Zur pathologischen Anatomie des Gihirns: II. Heterotopie der grauen Hirnsubstanz, Virchows Arch. f. path. Anat. **38**:138, 1867.

4. Ermann, F.: Heterotopie grauer Hirnsubstanz, Virchows Arch. f. path. Anat. **56**:419, 1872.

5. Hoffmann, E. K.: Ueber Heterotopia von grauer Hirnsubstanz, Ztschr. f. rat. Med. **34**:104, 1869.

6. Otto, R.: Zur Hirnpathologie, Virchows Arch. f. path. Anat. **110**:81, 1887.

7. Wicke, B.: Atrophie der rechten Grosshirn- und der linken Kleinhirn-Hemisphäre mit Heterotopie der grauen Substanz und Skoliose des Schädels, Deutsche Klinik **19-20**:175, 1898.

8. Matell, Magnus: Ein Fall von Heterotopie der grauen Substanz in den beiden Hemisphären des Grosshirns, Arch. f. Psychiat. **25**:124, 1893.

running from the cortex through this heterotopic mass. The brain was small and the basal nuclei were poorly developed. Meine [9] described another similar case and noted that the heterotopic mass contained ganglion cells with axis cylinders, but the cells and nuclei were very pale. In his case also there was metaplasia of the olive at the normal site of the ganglion of the fifth nerve. The ganglion cells of this mass had axis cylinders but no myelin sheaths. Probst [10] described some heterotopic islands in a case of microgyria and absence of the corpus callosum. In Freeman's [11] case, heterotopia was found in the meninges anterior to the pons. In many cases of tuberous sclerosis, heterotopic nodules similar to that described by Freeman [12] are found in the brain substance. Bielschowsky's [13] study is the most valuable and complete on the subject. He described a case similar to Meine's with olivary heterotopia and discussed the formation of heterotopic nodules. The anomaly was in an idiotic child; the brain was of normal size and weight but with practically no convolutions. He considered the case a combination of pachygyria and agyria. The main heterotopic mass was just underneath the cortex, and the pia was very vascular, especially over the areas of agyria. He discussed the formation of the cortex and its four primitive layers that were present in his case and also in cases of microgyria. The layers of cells of the cortex were similar to those of a fetus of about four months. He pointed out that three processes were necessary for the formation of normal cortex, migration, grouping and maturing of the cells. These processes take place between the fourth and sixth months, and any disturbance at this time produces malformations. He considered vascularity very important, and expressed the belief that the vascular anlage is defective and that fetal meningo-encephalitis completes the disturbance. However, rarely do any of the usual signs of inflammation remain. There is often increased vascularity over the areas of pachygyria, and often disturbances of the cortex are to be found under hemangiomas of the pia. Kotschetkowa [14] was the first to draw attention to the close connection

9. Meine, H.: Ein Beitraga zur Lehre von der echten Heterotopie grauen Hirnsubstanz, Arch. f. Psychiat. **30**:608, 1898.

10. Probst, Moriz: Ueber den Bau des vollständig balkenlosen Grosshirns sowie über Mikrogyrie und Heterotopie der grauen Substanz, Arch. f. Psychiat. **34**:709, 1901.

11. Freeman, Walter: Cortical Heterotopia in the Pontine Meninges, Arch. Path. **2**:352, 1926.

12. Freeman, Walter: Tuberous Sclerosis, Arch. Neurol. & Psychiat. **8**:614 (Dec.) 1922.

13. Bielschowsky, M.: Ueber Mikrogyrie, J. f. Psychol. u. Neurol. **22**:1, 1915; Ueber die Oberflächengestaltung des Grosshirnmantels bei Pachygyrie, Mikrogyrie und bei normaler Entwicklung, ibid. **30**:29, 1923.

14. Kotschetkowa, L.: Beiträge zur pathologischen Anatomie der Mikrogyrie und Mikrocephalie, Arch. f. Psychiat. **34**:39, 1901.

that exists between abnormal formation of convolutions and heterotopia. In a still later article, Bielschowsky and Rose [15] showed that pachygyria and agyria belong to the same type of disturbance and they thought that such conditions represent disturbances at a certain stage of fetal growth which prevents further development and differentiation. Bielschowsky [16] stated that the disturbing agent may be one of several, but he considered inflammation the most significant as it involves the blood supply. He also mentioned the importance of maternal toxins. He mentioned mechanical disturbances such as accidents to mother and fetus but thought them of less importance. Vogt [17] found hemangiomas and dilated capillaries over areas of microgyria and thought that the vascular disturbance is the basis of the malformation. Only a few authors have described cases of occlusion of the aqueduct of Sylvius which were considered congenital in origin. Most cases of occlusion have been described as sequelae of acute, subacute or chronic ependymitis, or as a proliferation of subependymal glia without any other inflammatory reaction.

In 1873, Magnan and Mierzejewsky [18] reported nine cases of paresis in which evidence of granular ependymitis was found on the ventricular walls. In one of their cases these granulations were present in a marked degree in the aqueductus cerebri and two opposing granulations had become adherent and had caused partial obstruction of the lumen. This obstruction had produced internal hydrocephalus of the lateral and third ventricles, while in the fourth ventricle there was only marked granulation and proliferation of the lining ependyma. This appears to have been the first case in which occlusion or partial occlusion of the aqueduct, due to ependymal changes, was recognized as the cause of hydrocephalus. Spiller [19] reported a case and noted collections of ependymal cells in the

15. Bielschowsky, Max; and Rose, Maximilian: Ueber die Pathoarchitektonik der mikro- und pachygyren Rinde und ihre Beziehungen zur Morphogenie normaler Rindengebeite, J. f. Psychol. u. Neurol. **38**:42, 1929.

16. Bielschowsky (footnote 13, second reference).

17. Vogt, Heinrich: Ueber die Anatomie das Wesen und die Entstehung mikrocephaler Missbildungen, nebst Beiträgen über die Entwickelungsstörungen der Architektonik des Zentralnervensystems, Wiesbaden, F. Bergmann, 1905.

18. Magnan and Mierzejewsky: Des lésions des parois ventriculaires et des parties sous-jacentes dans la paralysis générale (épendymite encéphalite, interstitiele diffuse péri-épendymaire), Gaz. méd. de Paris **45**:262, 1874; Arch. de physiol. norm. et path. **5**:531, 1873.

19. Spiller, W. G.: Two Cases of Partial Internal Hydrocephalus from Closure of the Interventricular Passages with Remarks on Bilateral Contractures Caused by a Unilateral Cerebral Lesion, Am. J. M. Sc. **124**:44, 1902. Spiller, W. G., and Allen, A. R.: Internal Hydrocephalus: Report of Two Cases, One Resulting from Occlusion of Aqueduct of Sylvius, Univ. Penn. M. Bull. **20**:1907-1908.

tissue surrounding the occluded aqueduct. He likened the changes in tissue around the occluded aqueduct to those sometimes seen in the region of the central canal of the spinal cord. Spiller is the only author who has mentioned such a similarity. He also showed the marked variations in the size of the aqueduct of Sylvius in supposedly normal persons.[20] Oppenheim [21] reported a case in which there was bridging of the aqueductus cerebri and Merle [22] had a case in which there was occlusion by an ependymal cyst. He thought the cyst was due to hydrops of a granule in granular ependymitis. Schlapp and Gere [23] had a series of five cases of occlusion of the aqueduct, and their illustrations show some of them to be similar to Spiller's case. There has been a considerable number of cases of occlusion of the aqueductus cerebri due to frank inflammation, both acute [24] and chronic.

In a recent study, Shelden, Parker and Kernohan [25] examined six cases of occlusion of the aqueductus cerebri. Of these cases, one was a case of acute ependymitis occurring in an adult, and five were in children between the ages of 7 and 15 years. Of these five, one showed signs of chronic subependymal inflammation, but in the others there were no signs of inflammation. The condition in several of the cases was like the occlusion of the central canal of the spinal cord as originally suggested by Spiller.

REPORT OF CASE

History.—A girl, aged 3 years, had hydrocephalus and epilepsy. The child appeared normal at birth but at 4 months was undernourished. However, her condition improved until the age of 1 year when she had several epileptic convulsions which continued intermittently until the time of her death. The child had never been able to speak or to walk, and although sensation was disturbed, she could hear a little and eat well. Her body was well nourished but the head was enlarged; the circumference was 56 cm.; the anteroposterior diameter was 19.5 cm., whereas the transverse diameter was 15.5 cm. The Wassermann reaction of the blood was negative, and the urine was normal. Lumbar punctures were done from time to time but they had no effect on the condition. She went into status epilepticus and died the following day.

Necropsy (Professor Jakob).—All organs of the body cavities were normal. On opening the skull, about 1,000 cc. of blood-stained fluid was found, and when

20. Spiller, W. G.: (*a*) Syringoencephalitis, Syringoencephalomyelitis. (*b*) The Function of the Pyramidal Tract, J. Nerv. & Ment. Dis. **44**:395, 1916.

21. Oppenheim, H.: Ueber eine Bildungsanomalie am Aquaeductus sylvii, Monatschr. f. Psych. u. Neurol. **7**:177, 1900.

22. Merle, Pierre: Étude sur les épendymites cérébrales, Paris, 1910, no. 305.

23. Schlapp, M. G., and Gere, Belden: Occlusion of the Aqueduct of Sylvius in Relation to Internal Hydrocephalus, Am. J. Dis. Child. **13**:461 (June) 1917.

24. Globus, J. H., and Strauss, Israel: Subacute Diffuse Ependymitis: Report of a Case Simulating Tumor of the Brain, Arch. Neurol. & Psychiat. **19**:623 (Dec.) 1928.

25. Shelden, W. D.; Parker, H. L., and Kernohan, J. W.: Occlusion of Aqueduct of Sylvius, to be published.

the brain was removed it had collapsed over the parietal regions (fig. 1). The tissue was very soft. The convolutions were irregular both in size and direction but did not appear to be either pachygyric or microgyric. The pia was more vascular than normal. A frontal section through the brain showed the walls of the hemispheres in some places to be only about 5 mm. thick. The lateral and third ventricles were greatly dilated and the septum pellucidum was almost completely absent. Scattered over the lateral and superior walls of the lateral ventricles there were numerous reddish-brown nodules. These were for the most part round, although some were slightly oval and projected partly into the ventricular cavities. They measured from 1 mm. to 1 cm. in diameter. No such nodules were present over the basal nuclei. Sections across the midbrain showed the aqueductus cerebri to be closed and the tissue in this region was gray and gelatinous in appearance. No exudate of any sort was present in the lateral or third ventricles. There was no hydrocephalus of the fourth ventricle, which was

Fig. 1.—Gross appearance of the brain, showing collapse of the walls of the cerebrum due to the escape of the cerebrospinal fluid from the distended ventricles.

quite normal, as was the medulla oblongata and cerebellum. There was no thickening or opacity of the meninges at any point. The brain weighed 930 Gm. and the capacity of the skull was 1,880 cc.

Anatomic Diagnosis.—There was hydrocephalus internus of the lateral and third ventricles. Heterotopic islands of gray matter were present in the ventricular walls. The aqueductus cerebri was occluded.

Microscopic Examination.—Histologic study showed the ependyma to be absent from the walls of the lateral and third ventricles, and there were no signs of inflammation in or beneath the subependymal glia. This glial zone was not uniform in width or in appearance. In most places it was wide, contained more than the normal number of cells, and a definite nonfibrillar reticulum was present which stained more deeply with toluidine blue than the adjacent white matter. Bielschowsky's stain showed that no axis cylinders were present in this layer. Occasionally, a few ganglion cells were found along its deeper boundary. In places this glial layer widened and became continuous with a heterotopic island or

else it divided so as to surround such a mass. These heterotopic nodules varied much in size and content; all were sharply circumscribed from the adjacent tissue (fig. 2), had a different reaction with toluidine blue strain from that of the surrounding structures and a similar reaction to that of the subependymal glia. These islands contained many ganglion cells without any definite arrangement; in no place did they show any laminations. The nerve cells were not normal, although many were pyramidal in shape; they varied much in size, and the bodies were pale and contained immature Nissl substance. Occasionally, small collections of neuroblasts were present. Bielschowsky's stain showed that axis cylinders were not present. There was an excessive number of glial cells but no glial fibrils could be demonstrated with the neurologial stain. With toluidine blue, the cell bodies stained very poorly. With van Gieson's stain, no excessive amount of con-

Fig. 2.—Heterotopic islands of cortical tissue in ventricular wall. The islands are different in staining reaction from that of the surrounding tissue and they are definitely circumscribed. The absence of ependyma from the ventricular wall is noteworthy.

nective tissue was present. There were no heterotopic islands over the basal ganglia nor on the undersurface of the corpus callosum.

Microscopically, the cerebellum, pons and medulla oblongata were normal. The meninges did not show any signs of inflammation either recent or old, and were normal.

As it is impractical to give a detailed description of the changes in all the separate convolutions, they will be presented in groups arranged according to the classification of Brodmann, and the most marked changes in architecture and cell structure mentioned.

In the frontal region, on its lateral surface, the cell layers were normally arranged, but on the superomedial and medial surface, the cells of the second lamina were collected into islands and consequently there were areas devoid of cells. The sixth lamina was irregular. Some cells were at distances of 6 mm.

in the white matter and almost down to the ventricular wall. The dendrons were poorly developed; the cell bodies were pale and many were vacuolated. In the subependymal zone there were collections of small round cells without demonstrable cell bodies, which appeared to be glial nuclei. In the same place as these cells was a considerable number of immature ganglion cells which were apolar, unipolar or bipolar and which contained little Nissl substance but normal appearing nuclei and nucleoli. In the basofrontal region, the laminae were normally arranged in some of the convolutions but in one convolution, the third and fourth laminae bent toward the white matter and the fifth and sixth laminae were sharply kinked on themselves. In other convolutions there were areas poor in cells giving a mottled appearance (fig. 3) and in still other convolutions the fifth and sixth laminae were compressed into a narrow band of cells, many of which were immature and had hypochromatic nuclei, small cell bodies and undifferentiated Nissl substance. In the posterior part of the midfrontal convolution a similar mottled

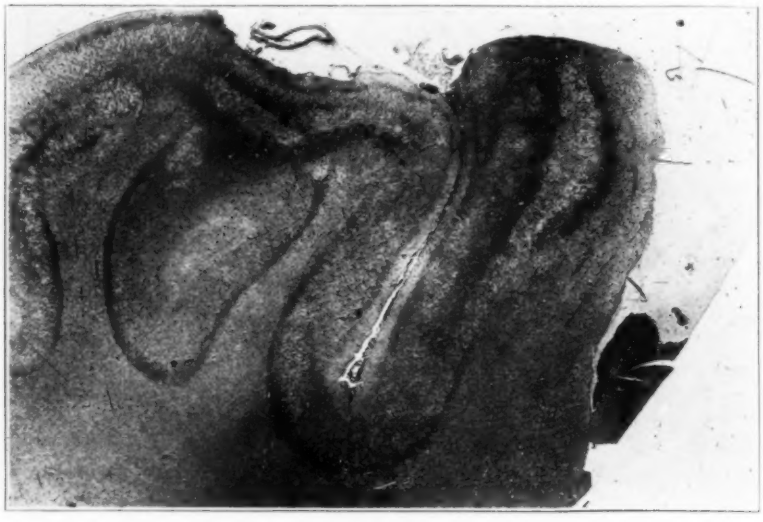


Fig. 3.—Mottled, irregular cortex showing the irregularities of the cortical laminations.

appearance was present. Here, in the third and fifth laminae, the cells were sparce and the reticular substance stained more lightly than the surrounding tissue. In the inferior frontal convolution, these comparatively acellular islands in the fifth lamina were so large as to cause distortion of the sixth lamina with disarrangement of its cells (fig. 4). In the superior frontal and upper part of the middle frontal convolutions, at their posterior ends, in the precentral region, the cortical wall was very thin and there were many heterotopic islands in the ventricular wall. The laminae were all present, but the cells were not evenly distributed and were collected into islands. Here and there, the fifth and sixth layers were represented by a narrow, irregular layer of immature cells. The nuclei were hyperchromatic and the nucleoli were enlarged and had indistinct outlines. The Nissl substance was pale and in minute granules, while the processes were tortuous and corkscrew-like in appearance and usually irregular (fig. 5). There was, also, an increased number of glial nuclei in this layer, probably the result of the compres-

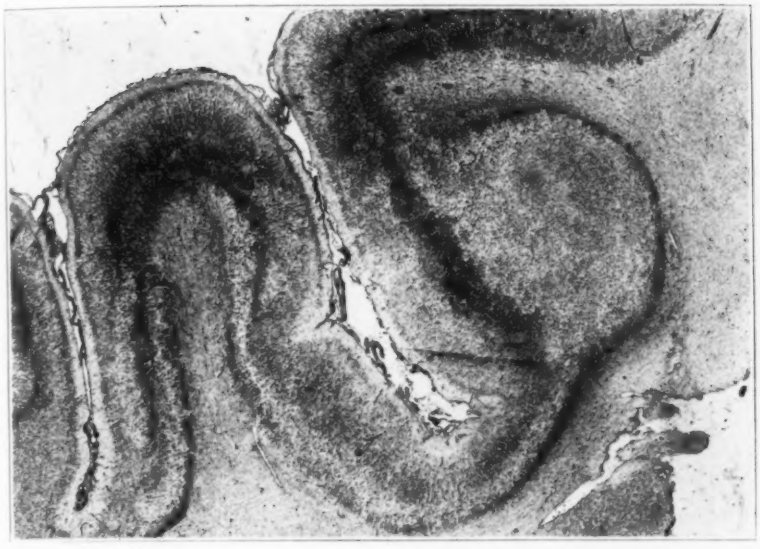


Fig. 4.—Abnormal appearance of the fifth and sixth laminae. There is a marked bulge in one place. There is also some mottling of the cortex due to unequal distribution of the cells in the various laminae.

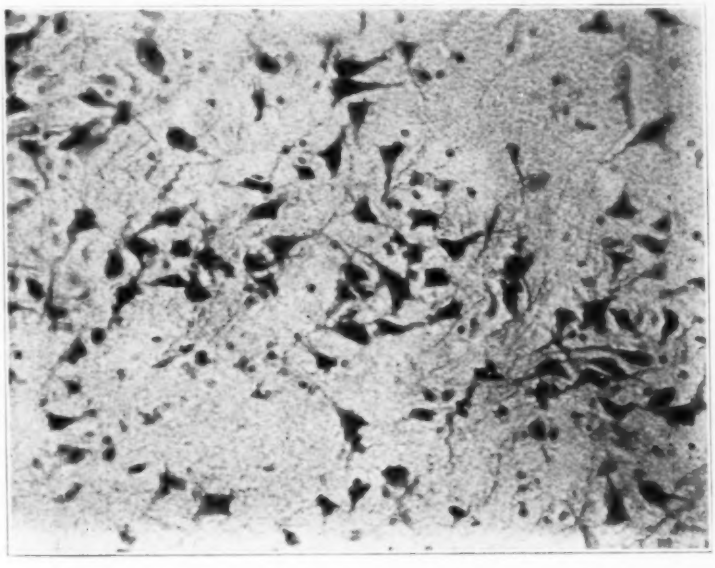


Fig. 5.—Cells of the sixth lamina showing them collected into a narrow band. The cell processes are irregular or corkscrew-like in appearance. These cells are either immature or degenerated; × 250.

sion or condensation. In the precentral region proper, in the precentral convolution, the laminae were normal in number and regular in arrangement. However, the cells of most layers were not normal, as the bodies contained very pale and sometimes vacuolated cytoplasm. The Betz cells of the fifth lamina were few in number and when found were often collected into groups. These cells, like the cells of the other laminae, had pale cytoplasm while the periphery of the nuclei was pale and the center stained deeply. The center was not like the normally dark, sharply circumscribed nucleolus. In some parts of the centrum semiovale, glial nuclei were collected into groups. In other places there were innumerable small, round or irregular, nucleated, homogeneous masses which had a pink reaction with the toluidine-blue stain. Many of these masses had processes streaming off into the surrounding tissue, and represented gemästete glia cells, while others were swollen oligodendroglia cells. There was definite degeneration of the myelin

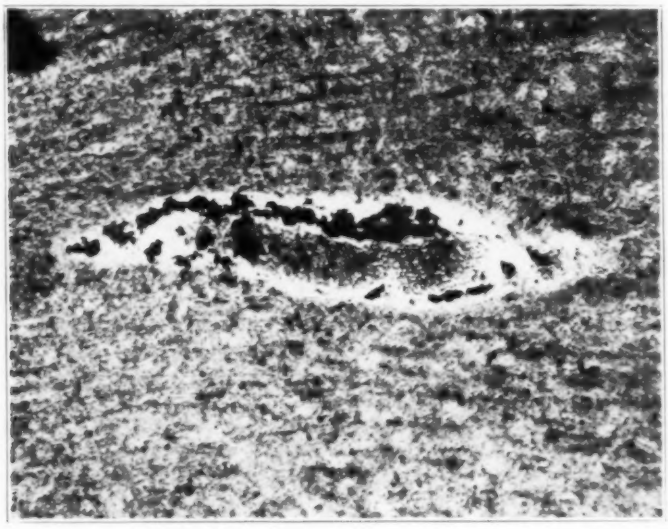


Fig. 6.—Perivascular collection of fat in the cortical rays. Scharlach r stain; × 125.

in this area and the scharlach r stain showed collections of fat in some of the perivascular spaces. These perivascular collections of fat were most abundant in the cones and radiations of the myelin into the cortex (fig. 6).

In the postcentral convolution, the laminae and arrangement of cells were normal. In most of the regio parietalis the cortical layers were present in normal number but not in normal arrangement. In the sixth lamina the cells were crowded into an irregular band; many of the cells were immature, with poorly developed processes or even no processes at all. There were many large nerve cells in all laminae except the first lamina and there were only a few in the second lamina. The cell type was different from that of the cells seen in the midbrain, in that the tigroid substance was in larger granules. These cells were quite prominent because of their size and staining reaction, but none was present in the white matter. At the juncture of the superior and medial surfaces, one convolution did not show the regular number of laminae, as the cells of the fifth and sixth layers were fused and diffusely scattered. The third layer was almost

devoid of cells and was conspicuous on this account. On the superior surface of the occipital region the cortical architecture was abnormal. Occasionally, the laminae were all present, but usually the cells were so disarranged that it was impossible to distinguish any laminations. There were groups of cells without any definite arrangement, and in other places the cells were few or even absent. On the medial surface, gyri were not present, and the wall of the hemisphere was thin. However, the laminations were all present, except in one place, where it was impossible to distinguish the sixth lamina. Although the laminations were present, the cells were immature; the majority were rounded rather than pyramidal. The glia in the white matter showed degenerative changes similar to those seen in the centrum semiovale. In the area striata, the laminae were normal, but many cells were immature; others were degenerated and few were normal. This was especially true of the deeper layers. Numerous large nerve cells were dis-

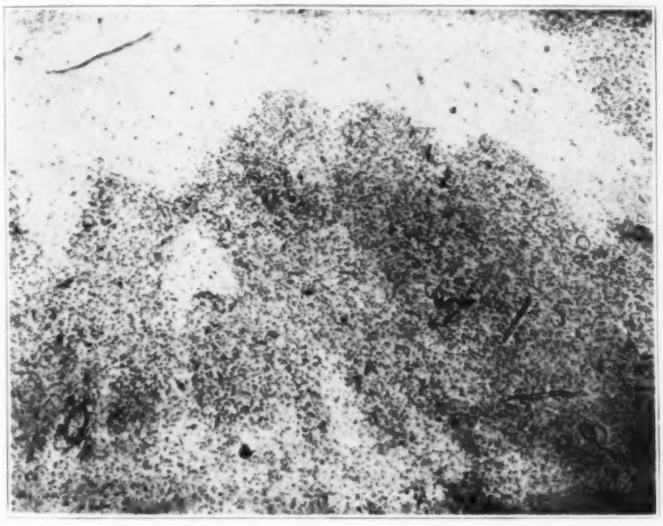


Fig. 7.—Irregularities of the first and third laminae with areas of rarefaction in the third lamina. The first lamina is broader than normal; × 15.

tributed throughout the fourth, fifth and sixth laminae but there were fewer in the second and third laminae, where the other cells were better developed. The juncture of the area striata to the occipital lobe was striking because of the fact that in the other convolutions of the occipital lobe, the laminae were irregular and malformed while in the area striata, the laminations were almost normal. There were degenerative changes of the glia in the optic radiations, similar to those noted in the centrum semiovale.

In the regio temporalis, the laminae and cell components were better developed and more clearly differentiated than elsewhere in the cerebrum. The formation of the uncus was unusual. There were remnants of the superficial granular layer underneath the pia, and below this, a broad lamina zonalis. In this lamina, there were many small, pale-staining nuclei, without demonstrable cell bodies, either scattered diffusely or collected into islands. The ganglion cells of the second lamina had a tendency to collect into groups but the attempt to form a zona glomerulosa was imperfect. At the juncture of the uncus to the basofrontal area,

there was a broad lamina zonalis with a narrow layer of cells underneath the pia mater. The second lamina was prominent as a broad irregular layer of glial cells and immature ganglion cells, and on the surface of this lamina there were numerous collections of pale-staining nuclei, without demonstrable bodies, namely, glial nuclei (fig. 7). The surface of this lamina was definitely indented, and in the third lamina, underneath, there was intermittent condensation and rarefaction of the cell distribution, but the appearance was not typical of microgyria. The fourth, fifth and sixth laminae were present, and between the sixth lamina and the ventricular wall were collections of cells forming islands. These collections of cells formed an irregular, accessory lamina which continued into the white matter of the temporal lobe. These cells were immature ganglion cells. The amygdaloid nucleus was flattened by the hydrocephalus, but between it and the sixth lamina of the uncus was a layer of ganglion cells collected into larger or

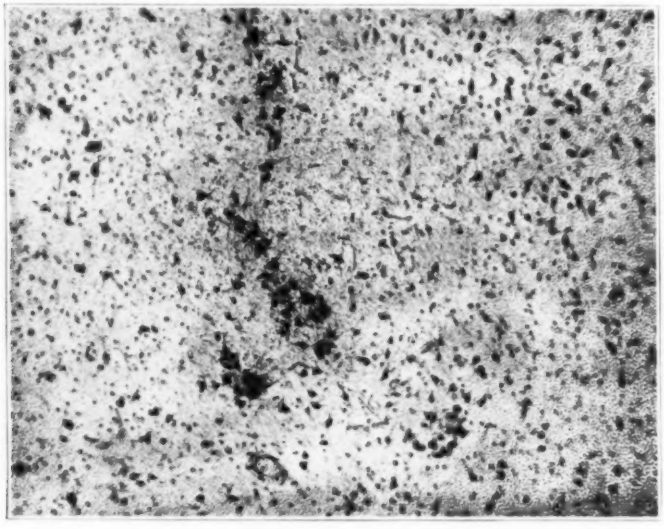


Fig. 8.—Islands of ganglion cells between amygdaloid nucleus and uncus. This is a heterotopic collection of cells; × 75.

smaller groups, similar to those situated between the uncus and ventricular wall (fig. 8). The majority of the cells appeared normal, although some neuroblasts were intermingled with them, and occasionally collections of glia nuclei also were present. This malformation suggests misplacement of the zona glomerulosa of the uncus, for that in the second lamina is very imperfect compared to the other layers. The hippocampus was of a primitive type and was similar to that depicted by Rose[23] for a human embryo of 10.5 cm. (fig. 9). There was a slight elbow-like bend in this primitive plate but it had none of the characteristics of the more fully developed ammon's horn formation. The cells also were primitive in type, with large nuclei and small bodies; there was little, if any, Nissl substance present, and when it was present, it was homogeneous. None of the cells had processes, and occasionally binucleated forms were seen; so it had more the appearance of proliferating cells than of normal ammon's horn formation. Occasionally, huge, better developed cells were seen, which were similar to the large

cells in other portions of the cortex that already have been described. The laminations of this area also were very primitive and contained four main layers of cells, but occasionally, in the intermediate zone, imperfect lamination could be distinguished. This zone was broad and the cells were similar to apolar neuroblasts; the nuclei almost filled the cell, while the cytoplasm was only a narrow ring. Some normal glia cells were intermingled with these primitive nerve cells. The structure of the insular cortex was abnormal. The first lamina was exceedingly broad, and just below the pia mater there was a narrow, acellular zone, followed by a very cellular zone that gradually diminished in density toward the nerve cell layer. The second and fourth laminae were completely absent and the third, fifth and sixth laminae were fused so that laminations were not present. Most of the cells of the insular cortex were pyramidal and occasionally were collected into small groups. The entire cortex was much thinner than normal, and

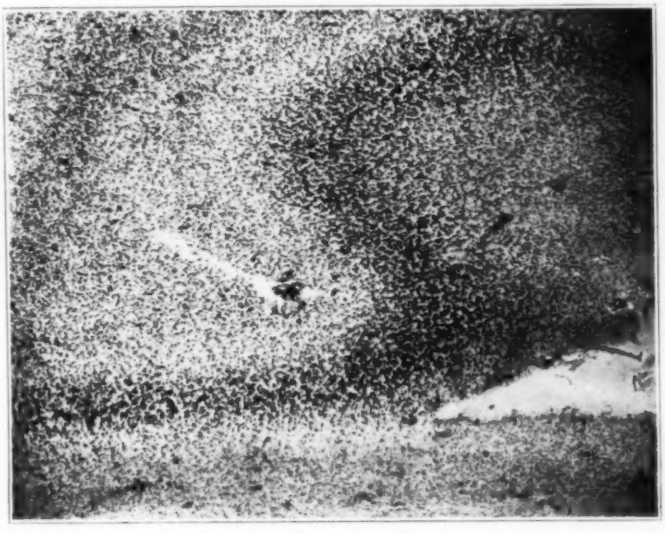


Fig. 9.—Embryonic type of ammon's horn formation. The characteristic curve is not present. Some of the cells are immature and some are large ganglion cells. An excessive number of cells is present; × 15.

there was an excess of glia nuclei. The Nissl substance in the nerve cells was incompletely differentiated, and despite the fact that most cells were pyramidal, none was normal. The cell type in the claustrum was normal, but again the cells were immature. The histologic structure of the basal nuclei was unusual. The thalamus was almost completely devoid of ganglion cells, and the few cells that were present were degenerative forms, that is, swollen cells with pale cytoplasm and evidence of neuronophagia. There were some neuroblasts present and an excess of blood vessels and capillaries as well as of glia cells of all sorts. The putamen had few normal ganglion cells, but there were many immature ganglion cells and neuroblasts. The caudate nucleus also had many small but immature ganglion cells, and few large ganglion cells, those present being degenerated. The caudate nucleus was similar to the putamen but different from the thalamus. In the subependymal glial zone, over the thalamus and caudate nucleus, there were remnants

of the primitive mother layer but no heterotopic islands. The corpus callosum was normal and heterotopic islands were not present on its inferior surface. There were some swollen astrocytes, but the myelin was normal.

Weigert's myelin sheath stain of large sections across the entire cerebrum, and also of smaller portions, showed that the myelin, in various parts of the brain, was not quite normal. Few of the myelin sheaths were regular but they had a varicose appearance. Swollen nodules were seen along the course of the myelin sheaths, the center of which stained less intensely or even failed to take the stain, so that they appeared as small rings. Such an appearance may be seen in the brain of a normal child but not in such excess as appeared here. The change in the myelin is most marked in the medullary rays, in which the scharlach r stain disclosed free fat in the perivascular spaces. Occasionally, in the centrum semiovale there were pale-staining areas in which the myelin sheaths were less numerous and were swollen, tortuous and ballooned in appearance. Large sections through the cerebrum showed evidence of marked internal hydrocephalus, and absence of the septum pellucidum. Heterotopic nodules were present on the ventricular wall, but not over the basal nuclei. These heterotopic regions are outlined by strands of myelinated fibers. With a higher power, a few fibers were seen to traverse the islands and divide them into smaller portions; however, these myelinated fibers were not scattered diffusely throughout the heterotopic masses. The basal nuclei contained a considerable number of myelinated fibers and the tail of the caudate nucleus was larger than normal. The myelin of the deeper layers of the cortex was unevenly distributed and had a mottled appearance like that seen with the toluidine-blue stain. Practically every myelin sheath of the deeper layers of the cortex was irregular, had a ballooned appearance and there were many places where the radiating fibers were absent or markedly reduced. The stripes of Baillarger were absent from most convolutions. With a low magnification, the myelin of the hippocampus was sparse and did not have its characteristic appearance; even, so, it was better differentiated than study of the thionine-stained sections would lead one to expect. However, with a higher magnification, the sheaths were seen to run in every direction throughout the ammon's horn formation and were irregular, nodular and ballooned. When blood vessels contained erythrocytes the cells stained deeply with Weigert's myelin sheath stain and in these sections the vessels and capillaries were seen to be more numerous than normal, especially in the ammon's horn formation, uncus and basal nuclei. Occasionally, around a vessel in the putamen, there appeared to be a "confusion" of the myelin sheaths; that is, the fibrils ran in every direction forming knots or islands around the vessels in contrast with the arrangement elsewhere in the basal nuclei. Throughout the entire cerebrum it was difficult to find what might be considered a normal myelin sheath.

In no part of its course was the aqueduct completely occluded but throughout its course it was very narrow (fig. 10). In general, the ependyma was apparently normal, and in only a few places was there any appearance of ependymal proliferation. At these points there was usually a second broad, diffusely scattered layer of ependymal cells separated from the aqueduct by a comparatively acellular zone of glia (fig. 11). In the quiescent places often small tubules or islets of ependymal cells were isolated from the aqueductal ependyma. Frequently, the subependymal glia projected upward, pushing the ependyma ahead of it or even herniating through it. These herniations, or projections, adhered to each other and cut off tubules of ependyma which later were disorganized and formed the islets. The proliferation and adhesions progressed and the ependymal rests separated further from the main duct, so that it gradually became narrower. The subependymal glial zone was quite narrow, contained very few cells, and the fibers

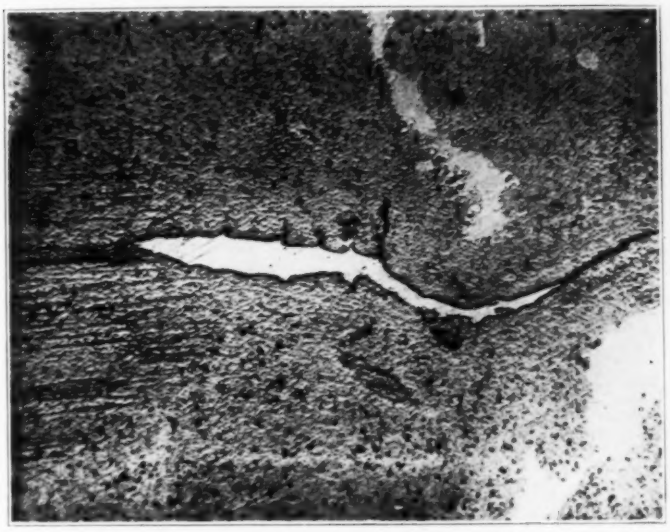


Fig. 10.—Narrow, elongated, slit-like aqueduct with comparatively quiescent type of ependyma and acellularity of surrounding tissue; × 40.

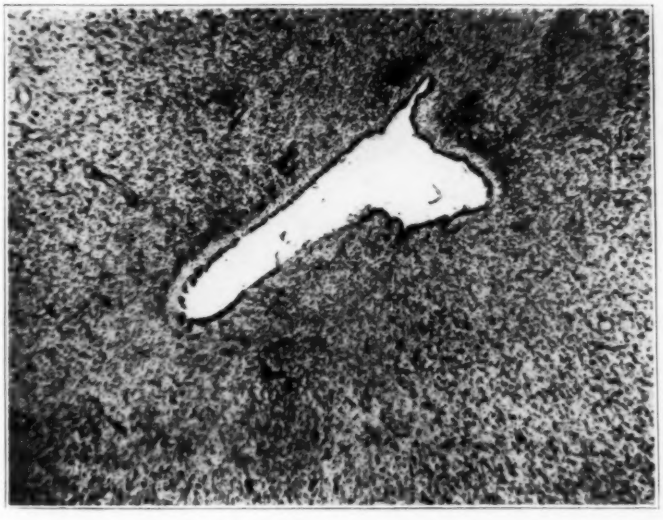


Fig. 11.—The small aqueduct of Sylvius. Ependymal activity and ependymal cells are evident in the subependymal glial zone. There is upgrowth of the subependymal glia, cutting off islands or tubules of ependyma. A comparatively acellular zone of glia is immediately below the ependyma; × 25.

were unstained by the victoria blue, glial fiber stain. In the tissue around the aqueduct, that normally is comparatively acellular, there was an increase in the number of nuclei. The majority were well formed and belonged to small, bipolar cells. Some, however, were unipolar, and others apolar, but most of them had immature tigroid substance in their cytoplasm. There was an excessive number of all sorts of glia cells but most of them were macroglia. Laterally from the aqueduct were small collections of large, globoid nerve cells (fig. 12) with deeply staining Nissl substance which, however, was in very fine particles and more abundant at the periphery of the cell. These cells had few processes, in many none at all, but in others one process was visible which was free from Nissl granules. These cells were not degenerated forms but were normally developed, even if of abnormal size and situation. They resembled much the cells seen in Clarke's

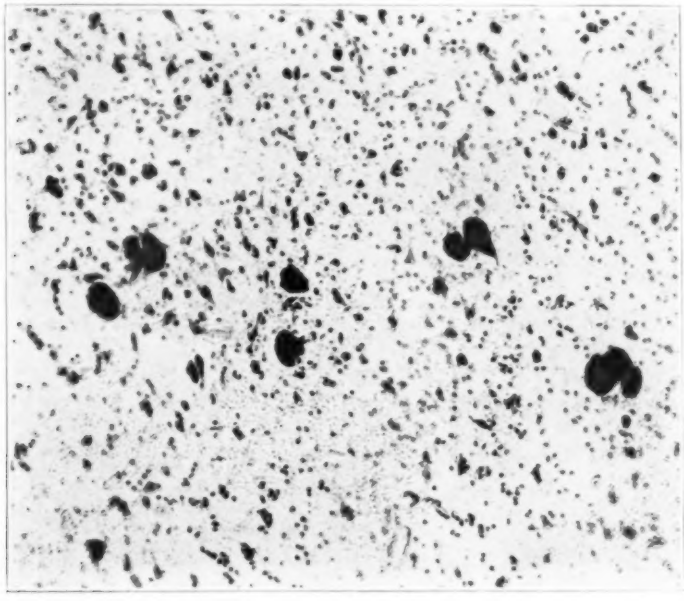


Fig. 12.—Large globoid nerve cells lateral to the aqueduct of Sylvius. The presence of very few processes is shown; × 115.

column of the spinal cord. Similar cells were scattered through the colliculi but there were none in the pons, which was normal. In the colliculi few of the nerve cells were normal; either they were immature or showed regressive changes. The most striking feature was the excessive number of cells, many of which were of glial type. There were many neuroblasts, which in some places were collected into groups or islands. Underneath the pia, in the molecular layer, there were massive collections of glia cells with large pale, swollen cell bodies and homogeneous-staining cytoplasm. Near the upper end of the midbrain the aqueductus cerebri divided into three separate canals, each one of which was very small and lined with ependyma. Between the most dorsal of the three tubules and the inferior pineal recess was a region of softening about 6 mm. long by 3 mm. wide. The center of the softened region was filled with cell débris and many compound granular corpuscles. The cavity had a definite wall, lined with swollen microglia

cells, but polymorphonuclear leukocytes were not present in the cavity, in its wall or in the surrounding tissue (fig. 13). In the last situation there were many transitional "körnchen" cells and also some fully developed forms. Some of these transitional forms were found close to the other divisions of the aqueduct. The posterior branch of the aqueduct was compressed by the softened area and was almost occluded.

In spite of the apparent proliferation of the subependymal glia, glia fibrils could not be demonstrated, but in the roof of the midbrain was a marked increase in the number of vessels, especially of the capillaries, which were widely dilated. There was no demonstrable increase in the connective tissue content of the midbrain or the region around the aqueduct. In the fourth ventricle the surface had the characteristic appearance of the so-called granular ependymitis; the ependymal cells were normal but the subependymal glia had proliferated, causing small nodules to appear on the ventricular wall. Below, and at the base of some of

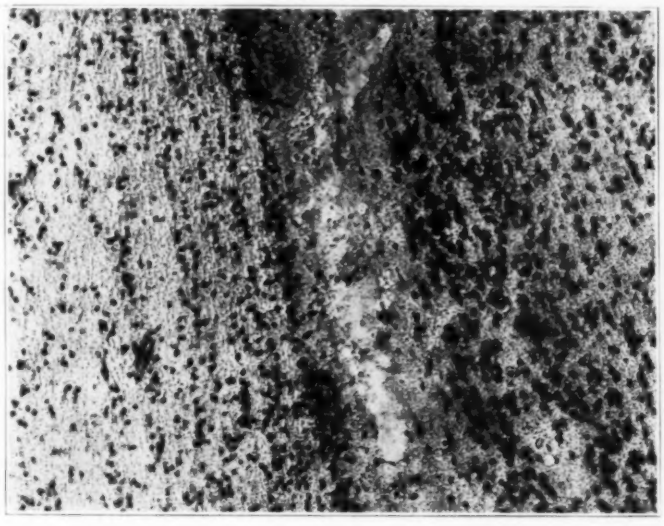


Fig. 13.—Edge of area of softening in roof of midbrain. Polymorphonuclear leukocytes are absent but large numbers of compound granular corpuscles can be seen. There is a definite wall about the area of softening; × 115.

these nodules, small masses of ependymal cells were scattered without definite arrangement. Other abnormalities were not seen.

There was no increase in connective tissue in the brain as demonstrated by the van Gieson and other stains. The larger blood vessels, for the most part, were normal, except a few in which appeared to be an increased number of nuclei in the adventitia or perivascular space. However, there was no change in the connective tissue of the vessels. In the smaller arteries and arterioles there was a slight increase in connective tissue in the adventitia as seen by the van Gieson stain. With toluidine blue, some medium-sized vessels were seen to have small groups of lymphocytes in the adventitial spaces and there was an excessive number of endothelial cells in the intima of some of the smaller arteries and arterioles. The media did not show any change and there was no increase of elastic tissue in any of the vessels. In the pia and arachnoid there was some evidence of old inflammatory reaction in the form of an increased number of cells and slight

thickening of the membranes. There was also a slight increase of connective tissue. Such minor changes did not furnish sufficient explanation of the anomalies in the cerebrum and midbrain and no real explanation is forthcoming unless it is assumed that Bielschowsky's theory of meningo-encephalitis at about from four to six months' gestation can be applied here. This, having subsided, leaves little evidence of its presence except the disturbance of the cellular arrangement and differentiation. The epithelial cells of the choroid plexus were, in many places, flattened rather than cuboidal, but in other places they were normal. Few cells had vacuoles, all had granules evenly distributed throughout the cells and the nucleus was centrally situated. In the middle of the papillae, here and there, were some large, epithelioid cells, with light-staining cytoplasm, which, with high magnification, contained innumerable small vacuoles. The nuclei often were kidney-shaped or oval and the cells probably were swollen endothelial cells, or, at any rate, of mesodermal origin.

COMMENT

Heterotopia of the nervous system is not common, but of the explanations for it that of Bielschowsky is the most logical. Bielschowsky,[16] backed by Rose's [26] studies, disagreed with Schaeffer [27] as regards the formation of the cortex and claimed that the heterotopic nodules in the subcortical white matter are a result of interference with cell differentiation and migration in an early stage of development of the organism. The cells migrate from the mother layer out toward the pia, and, due to the interference, some of the cells do not reach their normal site but form heterotopic nodules. Usually, in such cases, the convolutions are abnormally formed, as was first pointed out by Kotschetkowa; often the cortical layers are primitive as is seen in Bielschowsky's case of pachygyria and microgyria with heterotopia. In my case, the heterotopic masses may represent small groups of cells that were left behind when migration occurred, and differentiation of these cells may have taken place in this situation in the ventricular wall. Less probably, the explanation of the masses may be that while in the process of migration and differentiation, the disturbing factor caused an upset more in the migration than in the differentiation, and some cells instead of continuing outward toward the cortex wandered inward to the ventricular wall, where more complete differentiation occurred. Bielschowsky stressed the point that vascular disturbances are an

26. Rose, Maximilian: Ueber das histogenetische Prinzip der Einteilung der Grosshirnrinde, J. f. Psychol. u. Neurol. **32**:97, 1925; Der Allocortex bei Tier und Mensch: I, J. f. Psychol. u. Neurol. **34**:1, 1927; Die sogenannte Riechrinde beim Menschen und beim Appen: II. Allocortex bei Tier und Mensch, J. f. Psychol. u. Neurol. **34**:261, 1927; Die Otogenie der Inselrinde zugleich ein Beitrag zur histogenetischen Rindeneinteilung, J. f. Psychol. u. Neurol. **34**:182, 1928; Die Inselrinde des Menschen und der Tiere, J. f. Psychol. u. Neurol. **37**:467, 1928.

27. Schaeffer, Karl: Ueber normale und pathologische Hirnfurchung, Ztschr. f. d. ges. Neurol. u. Psychiat. **38**:1, 1917; Zum Mechanismus der Furchenbildung, ibid., p. 79.

important factor in the production of anomalies. He mentioned other factors, such as the occurrence of meningo-encephalitis in the migration period, which might disappear and leave no demonstrable trace. It is possible that some such factor was present here. There are here, also, the cortical anomalies often associated with heterotopia and these cortical disturbances represent arrest in differentiation of the cells in many places and also in their grouping. So there is disturbance of all three basic factors: namely, migration, maturation and grouping of the neurogenic elements. The period at which these factors occur is between the fourth and sixth months; Bielschowsky thinks that it is nearer the fourth than the sixth month. The formation of the ammon's horn in this case corresponds to that depicted by Rose [28] in a human embryo of 10.5 cm. The appearance of the cortex of the preoccipital region, on its medial surface, also corresponds to this period. The disturbance was thus widespread; only the pons, medulla oblongata and cerebellum escaped. The thalamus, according to Rose,[29] is formed from the same mother layer as that from which the cortex is formed; some of the mother layer remains behind and forms the thalamus. In this case the thalamus had few nerve cells and this means that most of the cells either migrated toward the cortex or else disappeared later than the time of migration. The putamen and caudate nucleus had a somewhat similar histologic appearance. Many small but immature ganglion cells and only a few large cells were present. According to Rose's [29] embryologic studies, the two structures develop in the same way and all the cells of the mother layer remain in position to form them, while the thalamus, which has fewer neurogenic elements, develops from only part of the mother layer. This embryologic difference is reflected in their present architecture. Probably a similar disturbance of migration can explain why only a few cells were normally situated in the lamina, and the remainder were situated between the sixth lamina and the glomerulosa of the amygdaloid nucleus, which itself was not normal.

The four layers that are characteristic of the microgyric brain, and in which the cells usually are quite well differentiated, were not seen anywhere in the cortex. Macroscopically, the gyri appeared smaller than normal, but microscopically, the structure did not correspond with any characteristic type of disturbance. Sometimes one layer, sometimes another layer, and occasionally all layers, were abnormal; seldom were they all normal. Throughout most of the cortex, the sixth layer was conspicuous because its component cells were crowded into a rather narrow band. Occasionally, however, cells from this layer were found

28. Rose (footnote 26, second reference).

29. Rose (footnote 26, third and fourth references).

in the white matter, as if they had lagged behind during migration. Even when grouping was complete, if it was not always normal, the differentiation of the cells in many places was immature, suggesting that the noxa which appeared about the fourth month had a prolonged action, although the glial and mesodermal elements were more normal. In addition to the developmental anomalies, there was definite evidence of degenerative processes. There was fat in some of the perivascular spaces. In the centrum semiovale, and in the optic radiations, there was swelling of the macroglia and oligodendroglia cells; there were also numerous corpora amylacea. Some of the macroglia cells had formed gemästete cells, and many had round bodies without processes and with homogeneously staining cytoplasm. In the fourth ventricle the ependyma, for the most part, was intact, but in the wall there was evidence of proliferation of the subependymal glia, with small projections upward, such as is seen in so-called granular ependymitis. At the edges of some of these nodules, ependymal cells were found in the subependymal glia zone and had the same appearance as that already described in a previous contribution;[25] namely, the glia proliferating upward and herniating through the ependymal lining, spreading laterally and covering up small masses of ependyma and forming tubules, small isolated islands or cells strewn diffusely in the tissue. This appearance was well seen in the region of the aqueduct and the method of formation was illustrated. So the process was not ependymal proliferation, but proliferation of the subependymal glia.

It is not always possible to correlate clinical data and pathologic studies, and this holds true in this case to a certain extent. However, there were disturbances of the Betz cells of the precentral convolution; these cells were not present in normal numbers, and when present, often they were collected into groups and many showed signs of degeneration. There were, moreover, degenerative changes in the medullary rays and in the centrum semiovale as well as extensive disarrangement of the cortical laminations. The patient could hear, and in spite of the extensive cortical disturbances, the most normal portions were the temporal lobes.

In this case, of the three factors—migration, grouping and maturation of the cells—that ordinarily lead to the formation of a normal brain, only one was visible grossly, namely, migration. In the histologic study, the next factor to be noted was grouping, but the most important factor was the immaturity of the neurogenic elements. This was more difficult to demonstrate, but was more extensive and more serious than the other two. Besides the immaturity of the cells, there were definite degenerative changes in the cells of the cortex and basal nuclei, which cannot be attributed to postmortem changes, as all cells were not involved

and those in the posterior fossa were normal. The mesodermal elements showed slight signs of old inflammation and in only three places was there any evidence of increased vascularity: in the midbrain, the ammon's horn formation, and the thalamus. A satisfactory basis was not found to explain the anomalies, nor was there any explanation of the degenerative changes found in the ganglion cells or of the glia changes in the centrum semiovale or in the optic radiations. In the occipital lobe, particularly in the area striata, there were many large ganglion cells in the deeper layers of the cortex, whereas in the more superficial laminae, these cells were less numerous or even absent. In the latter layers, the nerve cells were better differentiated than in the deeper laminae. The large cells generally were better differentiated than the other nerve cells, but because of their size and situation, they were abnormal. Throughout most of the cortex, the sixth lamina was conspicuous because of the cells occupying a narrow zone; their processes usually showed degenerative changes while in the bodies were immature. In some areas, the cortex had a mottled appearance, like localized edema, but histologically this was not substantiated. It was due to absence of cells and represented a disturbance of the grouping of the neurogenic and even of the glia elements.

It usually has been considered that occlusion of the aqueduct of Sylvius is the result of inflammatory reaction, although occasionally congenital factors are supposed to play a part, and Spiller considered seriously abnormal activity of the subependymal glia as a factor. He saw a similarity between the process around the aqueduct and that around the central canal of the spinal cord. The central canal of the spinal cord is supposed to remain patent throughout life, but when investigating the growth and development of the ventriculus terminalis, I noticed[30] that the lumen of the central canal became obliterated in many cases between the ninth and seventeenth years of life and that the process was one of subependymal overgrowth. The appearance of the tissue in cases of obliteration of the lumen of the central canal is almost identical with the appearance in occlusion of the aqueduct in many cases in children. Embryologically, the central canal of the cord is analogous to the aqueduct of Sylvius, and what normally occurs in the central canal may occasionally occur in the aqueduct with serious results. I think that this is the explanation of the occlusion of the aqueduct in this case as well as in some of the cases that I studied with Parker and Shelden. In addition, in this case there were congenital anomalies which would tend to lead to the supposition that the occlusion was congenital. However, the child's head was normal at birth, and for some time

30. Kernohan, J. W.: The Ventriculus Terminalis, Its Growth and Development, J. Comp. Neurol. **38**:107, 1924.

afterward, so that the occlusion was progressive, the aqueduct slowly becoming narrower and hydrocephalus slowly developing. In all probability in most cases of occlusion of the aqueduct in children some congenital factor is the basis of the subependymal glial proliferation, but it cannot be assumed that the aqueduct is formed in as narrow a form as it is seen in histologic study. The occlusion may be completed at any time up to, or even after, puberty. The region of softening between the aqueduct and roof of the midbrain probably was a terminal occurrence and produced an acute exacerbation of the hydrocephalus. No explanation of this softening was found, but it was not inflammatory and was probably on a vascular basis. In only one place was there any evidence of ependymal activity combined with subependymal glial proliferation. The changes were similar to those described in a previous contribution,[25] in which subependymal activity was seen over the entire ventricular surface. In no part of the brain was there any sign of inflammation, so that this process cannot be classified as ependymitis, as is frequently done. Moreover, there was little increase of the mesodermal elements or of the fibrous glia. Despite the excessive number of cells in the roof of the midbrain, especially in the colliculi, they did not appear to occlude the aqueduct, and the tissue anterior to the aqueduct was normal. The cells in the roof of the midbrain were immature forms, but on the one hand they could not be considered neoplastic, nor, on the other, a heterotopic mass. It seems as if at one stage of differentiation and migration, something brought about arrest, and the cells remained thus immature and without normal arrangement. This applies to all the cells, both glial and neurogenic in type. Some cells had completely differentiated, yet they were abnormal for their situation in the midbrain.

SUMMARY

This is the case of a child who was afflicted with hydrocephalus, epilepsy and idiocy. The histologic study shows that three types of anomaly were represented: occlusion of the aqueduct of Sylvius, heterotopia on the ventricular wall, and disturbance of the normal arrangement of the cortical laminations, as well as immaturity of the neurogenic elements. The study does not supply a satisfactory explanation of the etiology of the condition, but a few signs of the old inflammation lend support to the theory that many cerebral anomalies may be produced by meningo-encephalitis which occurs during gestation. The cortical disturbance was extremely widespread; only the structures in the posterior fossa were normal. It is probable that all three types of anomaly spring from a common origin. The histologic appearance of the aqueductus cerebri is similar to that in many cases hitherto described, and the congenital factor must be considered.

POSTVACCINAL (COWPOX) ENCEPHALITIS

A CLINICOPATHOLOGIC REPORT OF A CASE *

GEORGE B. HASSIN, M.D.

Professor of Neurology, University of Illinois College of Medicine; Histologist to the Illinois State Psychopathic Institute; Attending Neurologist, Cook County Hospital

CHICAGO

AND

J. C. GEIGER, M.D.

Associate Professor of Epidemiology, University of California Medical School

SAN FRANCISCO

Cerebrospinal complications following antismallpox vaccination possess sufficiently characteristic pathologic features to be termed postvaccinal or cowpox encephalitis. In addition to the well known types of encephalitis, such as the epidemic (lethargic), hemorrhagic, syphilitic, and the ones complicating typhus fever, poliomyelitis and other infectious diseases, one should recognize also an encephalitis caused by cowpox. Thoroughly studied first (1912) but not published by Turnbull and McIntosh [1] in England, such complications were described in 1925, in detail, by European investigators, Luksch [2] in Czechoslovakia and Bastiaanse [3] in Holland. The pathologic studies by Turnbull and McIntosh, Bouman and Bok,[4] and especially Perdrau [5] are so complete that little can be added. In general, the literature pertaining to this apparently new morbid condition and covering its various phases—clinical, epidemiologic, immunologic and bacteriologic—is extensive. It has been repeatedly referred to in the editorials, letters

* Submitted for publication, Sept. 2, 1929.

* From the Pathologic Laboratories of the Research and Educational Hospitals, University of Illinois and the State Psychopathic Institute.

1. Turnbull, H. M., and McIntosh, J.: Encephalo-Myelitis Following Vaccination, Brit. J. Exper. Path. **7**:181, 1926. McIntosh, J., and Scarff, R. W.: The Histology of Some Virus-Infections of the Central Nervous System, Proc. Roy. Soc. Med. Sec. Path. **21**:705, 1927, pt. 1.

2. Luksch, F.: Blatternimpfung und Enzephalitis, Med. Klin. **20**:1170 (Aug. 24) 1924; Giebt es beim Menschen eine Vakzine-Encephalitis? Centralbl. f. Bakteriol. **96**:309, 1925.

3. Bastiaanse, Van B.; Bijl, J., and Terburgh, J.: Encéphalite consécutive à la vaccination antivariolique, Bull. de l'acad. de méd. Paris **94**:815 (July 21) 1925.

4. Bouman, L., and Bok, S. T.: Die Histopathologie der Encephalitis Postvaccinationem, Ztschr. f. d. ges. Neurol. u. Psychiat. **111**:495, 1927.

5. Perdrau, J. R.: The Histology of Postvaccinal Encephalitis, J. Path. & Bact. **31**:17, 1928.

and abstracts of the *Journal of the American Medical Association*.[6] The reasons for recording the present case are that it was the first observed (1926) in this country, though for certain reasons not published at the time; that it had a peracute, fulminating course, death having occurred in about thirty-one hours after the nervous symptoms set in, and that clinicopathologic studies of very early cases such as this may enable one to get a proper idea of the nature and evolution of the disease process. Aside from these considerations, the clinical picture itself was of interest.

REPORT OF CASE

History.—A white boy, aged 7, of Polish parentage, was admitted to the pediatric service of Cook County Hospital on Jan. 5, 1926, with the diagnosis "tetanus." About two weeks prior to admittance, the patient had been vaccinated against smallpox. For eleven days he had been feeling well, but on the twelfth day he began to complain of severe frontal headache and became bedridden. When admitted to the hospital the next day, he had several convulsions and suffered from lockjaw. The previous and the family histories were unimportant.

Examination.—The patient was an anemic child with a recent vaccination scar over the left arm. The condition of the surrounding skin is not mentioned in the records. The head was retracted and rigid; the mouth was firmly closed, and because of the marked trismus he could not open it. The teeth were carious and the gums were inflamed. The pupils were dilated and reacted to light and in accommodation. The cervical glands were enlarged. The lungs, heart and abdomen appeared normal.

The upper extremities were spastic, but the tendon reflexes were normal. The temperature was 99.8 F.; the pulse rate was 124, and the respiration rate 24.

A tentative diagnosis of atypical tetanus, with toxic convulsions, was made. Ten thousand units of a tetanus antioxin was given intramuscularly and an equal amount intravenously.

Course.—On Jan. 5, 1926, at 10:50 p. m., marked convulsive twitchings of both arms, the face and the upper part of the body occurred; the patient did not respond to questions. The teeth were firmly fixed; the axillary temperature was 99.8 F.; the pulse rate was 120, and the respiration rate 24.

On Jan. 6, 1926, at 8:30 a. m., the temperature was 107.7 F.; the pulse rate 168, and the respiration rate 68. The lungs were full of loud, moist and coarse râles. A blood count showed 26,000 white cells per cubic millimeter. Spinal puncture yielded a clear fluid, under normal pressure. The Pandy test for globulin was negative, and the number of the cells in the spinal fluid was "unincreased."

At noon the condition was poor, and respiration was labored; the patient was stuporous, and trismus as well as the reflexes had disappeared.

At 5 p. m., there were involuntary evacuations, the temperature was 104.6 F. (axilla), respiration was deep and labored, and mucous râles were present in the throat. At 7:10 p. m. the eyes were turned upward, and death occurred at 9:30 p. m., twenty-three hours after admission.

---

6. Postvaccinal Encephalitis, editorial, J. A. M. A. **92**:392 (Feb. 2) 1929; (June 15); Nonpurulent Encephalitis in Children, Berlin letter, ibid. **92**:2039 (June 15) 1929; Vaccination Encephalitis, London letter, **93**:391 (Aug. 3) 1929.

Histologic Observations on the Brain.—The histologic observations are given here in a general summary, only the most outstanding features being emphasized; the details as to the particular parts of the brain involved, which have been studied by others, are here omitted to avoid repetition.

Blood Vessels: The brain appeared very vascular. The blood vessels, especially the veins and the capillaries, were distended and hyperemic; some were thrombosed and some were surrounded by hemorrhages. The perivascular and adventitial spaces of the larger blood vessels were mildly infiltrated (fig. 1). Very

Fig. 1.—Cortex: A hyperemic vein showing a well defined adventitial space, mildly infiltrated. Outside, especially to the right, is the extra-adventitial cell infiltration; this is better shown in figure 3. The colorless cell bodies containing central dark nuclei are swollen oligodendroglia cells. Alzheimer-Mann stain; × 240.

few of the infiltrating cells were lymphocytes; plasma cells were absent, while the majority were similar to the cells that lay outside the adventitia where they formed extra-adventitial infiltrations. These consisted of nuclei—round, oval, kidney or horseshoe-shaped; some nuclei had an abundance of cytoplasm, while some appeared as gitter cells. The majority, however, appeared as naked nuclei,

very poor in chromatin and irregularly scattered over the parenchyma. Stained with silver carbonate, according to the method of Hortega, the nuclei appeared exceedingly pale and showed neither cytoplasm nor processes. In figure 2, the adventitial infiltration (*A*) is sharply bordered by the connective tissue adventitial membrane. It is clearly divided from the adjacent extra-adventitial infiltrations (*Ex*) which appear somewhat indistinct and pale. Their borders are merged with the surrounding parenchyma which is preserved and in the picture appears darker. In some instances, however, the adventitial and the extra-adventitial areas were

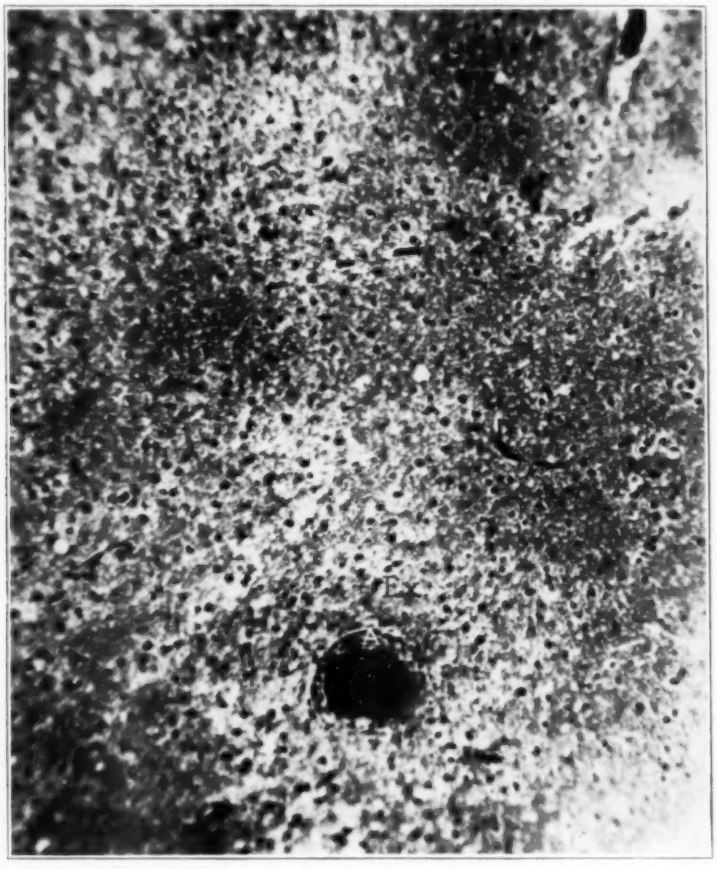


Fig. 2.—The vein in the lower half of the picture is hyperemic; its adventitial (perivascular) space (*A*) is enveloped, sleevelike, by the adventitia and is slightly infiltrated; the pale areas outside the adventitia are the extra-adventitial infiltrations (*Ex*) bordered by dark (normal) parts of the brain. Hortega silver carbonate stain; × 160.

less distinct, appearing as a whole, merged with one another. It is to be noted that the capillaries exhibited no infiltrations; these were confined to the larger blood vessels. However, the capillaries were hyperemic; their endothelium was prominent and the adventitial cells were hypertrophied, though poor in chromatin.

Each blood vessel, hyperemic, thrombosed and, surrounded by a double layer of infiltration, appeared as a distinct island (fig. 3). In some instances the islands were very numerous and so dense that the field appeared entirely covered by them. Often they coalesced, causing extensive and diffuse areas of infiltration (fig. 4).

Parenchyma.—Those parts of the parenchyma which were not covered by the islands, that is, were not invaded by the infiltration cells, were rarefied, reticular or vacuolated. They exhibited wide meshes which were covered by so-called

Fig. 3.—Typical islands of infiltration with invasion of the parenchyma around the hyperemic blood vessels. The adventitial and extra-adventitial infiltrations are merged. Hematoxylin and eosin stain; × 190.

swollen oligodendroglia cells (fig. 4)—dark vacuolated cell bodies containing nuclei rich in chromatin and surrounded by a granular membrane; the vacuoles were bridged by very delicate septums. In the extra-adventitial areas of infiltration themselves, meshes or vacuoles were absent. In these areas also were found no traces of axons or myelin, regardless of the staining methods employed (Alzheimer-Mann, Bielschowsky or both methods combined). The same methods however, showed an excellent preservation of the nerve fibers outside the zones

of infiltration, though in some instances the myelin sheath appeared slightly fenestrated and tumefied.

Of great interest also was the condition of the microglia. Represented in the extra-adventitial area of infiltration by gitter cells, they showed different changes in the preserved areas (fig. 5). They were invariably swollen and hypertrophied, and the processes were markedly tumefied, plump, shortened and fewer in number; in some instances they were reduced to a bipolar sausage-like formation (fig. 5, above in the left half of the picture); their nuclei were hypertrophied and

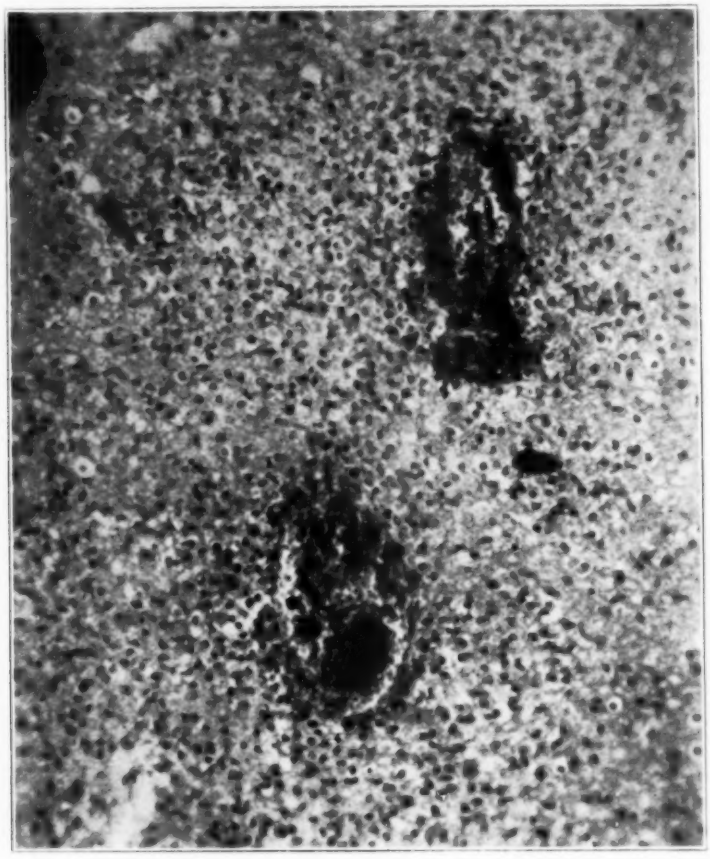


Fig. 4.—Areas of diffuse glial infiltration; numerous swollen oligodendroglia cells, better seen in figure 1. Alzheimer-Mann stain; × 90.

appear pyknotic in the picture, though under the microscope they were unusually pale. In the cortex itself, the microglia cells were much more numerous; they occasionally enveloped the ganglion cells which generally appeared normal. With ordinary cell-staining methods, they showed no changes in their configuration or staining qualities; nor did they show phenomena of satellitosis and neuronophagia. In general, the gray matter was less involved than the white.

Subarachnoid Space.—The subarachnoid space was much distended (fig. 6). Its meshes were of an enormous size and contained numerous mesothelial cells,

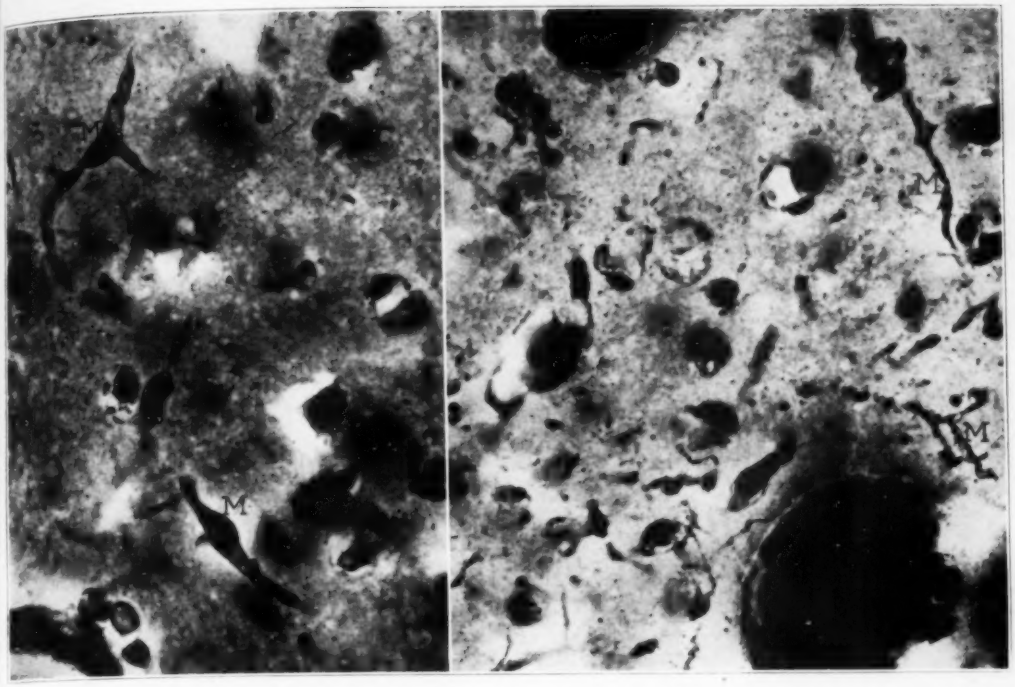


Fig. 5.—Swollen microglia cells (*M*). Other formations (oligodendroglia, for instance) are less distinct. Hortega silver carbonate stain; × 750.

Fig. 6.—The subarachnoid space: The pia is detached (artefact) and is unusually vascular. Hematoxylin and eosin stain; × 22.

fibroblasts, lymphocytes, polyblasts and macrophages, many of them packed with blood pigment.

Summary: The histologic changes that have been described occurred within thirty-one hours after the onset of the nervous symptoms. Despite so short a period of time, they showed extensive degeneration of the perivascular nerve fibers of the brain (the cord was not available), mild intra-adventitial parenchymal infiltrations, and hardly any evident ganglion cell changes.

COMMENT

The clinical picture in this case was that of tetanus. This was also true in the cases of Luksch, Wiersma,[7] and Wilson and Ford.[8] It is generally conceded (Mader)[9] that the tetanus type of postvaccinal encephalitis is the most malignant, and for this reason gives a grave prognosis. The condition may also progress as a tuberculous meningitis (Priesel),[10] a poliomyelitis, an encephalomyelitis or an obscure form of general intoxication. In about 50 per cent of cases it ends in recovery. In general, the clinical picture of postvaccinal encephalitis is not uniform; often it is not typical enough even to suggest an encephalitis. In contrast to the lack of uniformity of the clinical manifestations, some pathologic features are typical. One such feature is the zone of massive glial infiltrations around the blood vessels, where the nerve fibers are destroyed. The remarkable destruction of the nerves that takes place in an incredibly short time, has an analogy in the equally rapid nerve destruction observed in poliomyelitis. In the latter, however, the ganglion cells—that is, the gray matter—are principally affected, while in postvaccinal encephalitis the destruction affects mainly the white substance. In poliomyelitis, the cell destruction is associated with enormous hematogenous adventitial infiltrations, while in postvaccinal encephalitis the nerve fiber destruction is associated with equally excessive extra-adventitial glial infiltrations. As the latter, being practically devoid of nerve fibers, appear pale when stained with the methods of Weigert-Pal, Perdrau calls them areas of demyelination. Turnbull and McIntosh termed them areas of softening. Neither of these terms is altogether exact, as in the degenerated areas not only is the myelin but the axons are also for the most part destroyed. Nor are they softened, though a few gitter cells are present scattered among

7. Wiersma, D.: Encephalitis after Vaccination, Acta psychiat. et neurologica **2**:166, 1927.

8. Wilson, R. E., and Ford, F. R.: The Nervous Complications of Variola, Vaccinia, and Varicella with Report of Cases, Bull. Johns Hopkins Hosp. **40**: 337, 1927.

9. Mader, A.: Vakzination und Nervensystem, Jahrb. f. Kinderh. **123**:111, 1929.

10. Priesel, R.: Beitrag zur Encephalitis post Vaccinationem, Ztschr. f. Kinderh. **47**:152, 1929.

masses of glia cells which predominate. At any rate, such areas of extensive and intensive extra-adventitial infiltrations are not seen in any other type of encephalitis. It is most likely that they occur only in grave cases and are absent or insignificant in mild cases ending in complete recovery. This would be impossible if areas of demyelination or "softening" were present in every case. If extra-adventitial infiltrations are present also in mild cases, they must of necessity be very slight, probably represented by a moderate increase in the number of glia nuclei.

As myelin degeneration or demyelination is also an early and constant feature in multiple sclerosis, it was suggested (Perdrau, Pette [11]) that these two processes are alike. It was also claimed that such changes occur in measles, smallpox, varicella (Wilson and Ford) and whooping cough. One of us (G. B. H.) saw them also in a case of tuberculoma of the spinal cord. However, such changes in the conditions mentioned are generally rare. They have been so little studied and their histologic description is so incomplete that they can be ignored. The descriptions, for instance, of the cerebrospinal complications in smallpox given by Westphal,[12] Spiller,[13] Eichhorst,[14] Oettinger and Marinesco [15] are for the most part clinical (Westphal [1872]); pathologically, they differ from what is seen in postvaccinal encephalitis so much that it is hardly possible to detect any resembling features. As to the similarity to so-called acute multiple sclerosis, one should bear in mind that the existence of such a clinical entity is highly questionable; judging from the descriptions in the literature, one deals here with a disseminated encephalomyelitis or probably a complication of multiple sclerosis by some inflammatory condition, as in a case of Wohlwill.[16]

The histologic changes seen in postvaccinal encephalitis are definite and, as stated, occur within a very short period of time; they follow a uniform incubation period of about ten or eleven days, and run a rapid, fulminating course, ending either in complete recovery or in death. In these and especially in the histologic features the postvaccinal type of

11. Pette, H.: Das Problem der postvakzinalen Encephalitis, München. med. Wchnschr. **75**:207 (Feb. 3) 1928; Die Stellung der postvakzinalen Encephalitis in der Reihe infektiöser Erkrankungen des Zentralnervensystems, Centralbl. f. Bacteriol. **110**:134, 1929.

12. Westphal, C.: Ueber eine Affection des Nervensystems nach Pocken und Typhus, Arch. f. Psychiat. **3**:376, 1872; **4**:335, 1874.

13. Spiller, W.: A Report of Two Cases of Paraplegia Occurring in Variola, Brain **26**:424, 1903.

14. Eichhorst, H.: Ueber Erkrankungen des Rückenmarks bei Menschenpocken, Deutsche Arch. f. klin. Med. **111**:1, 1913.

15. Oettinger and Marinesco, G.: De l'origine infectieuse de la paralysie ascendante aigüe ou maladie de Landry, Semaine méd. **15**:45, 1893.

16. Wohlwill, F.: Zwei seltene Komplikationen bei multipler Sklerose, J. f. Psychol. u. Neurol. **37**:408, 1928.

encephalitis differs from other forms, such as the epidemic type, for instance.

The question naturally arises whether both the clinical picture and the histologic changes are not due to the vaccination. On this point, a great variety of opinions exists. McIntosh and Turnbull, Luksch (in his first publication, in 1924), Gorter and van Nederveen,[17] and Bijl[18] held the vaccination directly responsible for the encephalitis, while Bastiaanse, Levaditi and Nicolau,[19] Pondman,[20] Keller,[21] Pette did not. The occurrence of cerebral complications has been ascribed to various factors: activation by the vaccine of some micro-organisms (*Bacillus bipolaris*, for instance, according to Pondman and Pette); that vaccination produces encephalitis only in persons who were carriers of the germs that lay dormant and have been aroused or activated by the vaccination; that the "germ" of postvaccinal encephalitis is altogether different from the one that produces smallpox (Levaditi and Nicolau); that the vaccination reduces the defensive forces of the organism which harbors some infection, which may be that of poliomyelitis, epidemic encephalitis, herpes encephalitis, etc. It was also assumed that the vaccine virus combines with one that is in a latent state and produces an entirely new disease process; that is to say, the clinicopathologic features become modified because of the vaccination. On the other hand, Keller, Rivers[22] and others saw the cause of postvaccinal encephalitis in allergy or parallergy. The latter is assumed to enable a latent or intercurrent virus or a toxic agent to associate itself with the tissue especially affected. Whatever the explanations given, however ingenious they may be, the fact remains that if vaccination had not been used in some cases, complications followed by death would not have taken place. The fact also remains that postvaccinal encephalitis possesses specific features—a definite incubation period and a rapid course, and in about 50 per cent of cases gives a complete recovery, not followed by complications or sequelae. Such peculiarities are possible, according to Levaditi, because the vaccination virus so changes the type and virulence of the morbific agent that the very type of the pathologic changes themselves is affected. He also stated that the pathogenic germ may abandon the cutaneous area inoculated, invade the

17. Gorter, E., and Van Nederveen: Ueber unsere Kuhpockenimpfung. Abstr., Zentralbl. f. d. ges. Hygiene, **17**:63, 1928.

18. Bijl, J. P.: Die bisherigen Erfahrungen über Encephalitis nach Schutzpockenimpfungen, Zentralbl. f. d. ges. Hygiene **17**:449, 1928.

19. Levaditi, C.; Nicolau, S. N., and Sanchis Bajarri: L'étiologie de l'encéphalite post-vaccinale, Presse méd. **35**:1611 (Feb. 5) 1927.

20. Pondman, A.: Abstr., Zentralbl. f. d. ges. Hygiene **17**:64, 1928.

21. Keller, W.: Ueber Erkrankungen des Zentralnervensystems in Anschluss an die Kuhpockenimpfung, Nervenarzt **1**:729, 1929.

22. Rivers: Viruses, J. A. M. A. **92**:1147 (April 6) 1929.

"neuraxis" and produce an encephalopathy. The vaccine virus is thus, according to Levaditi, neurotropic.

The opinions quoted are mainly pure hypotheses and for the most part highly unsatisfactory. As Rivers justly remarked, "the chief objections to them (hypotheses) are, first, the necessity of assuming the presence of an unknown latent virus in such a variety of hosts as human beings, dogs and rabbits, and second, the improbability that such diverse incidents as vaccine virus and normal brain tissue acting in combination with an unknown virus in different species of animals are capable of causing a constant clinical and pathologic picture." We may add that the hypotheses quoted altogether minimize the rôle of the vaccination itself as an etiologic factor, considering it of secondary importance and, as Bastiaanse and Luksch (the latter in his first report) stated, that vaccination has nothing to do with the cerebrospinal histologic changes. The latter are generally considered the result of some latent microbic infection. However, the lack, even in very early stages as in our case (about thirty-one hours), of hematogenous infiltrations, which are so abundant in some infections of the central nervous system (poliomyelitis, epidemic encephalitis, syphilitic lesions, etc.) or parasitic invasions (trichiniasis, for instance) [23] would suggest that one deals here with a different type of lesion.

As noted, the principal pathologic feature was the extra-adventitial glia cell infiltration, probably as a reaction to a local nerve destruction, while the adventitial or so-called perivascular infiltrations were insignificant and practically devoid of hematogenous cells. The changes here described may be considered an acute stage of what is commonly seen in subacute or protracted toxic conditions of the brain. Bailey [24] gave a clear picture of an extra-adventitial glia cell accumulation (glia wall) in a case of encephalitis that clinically presented the appearance of a brain tumor. I have seen them in the specimens of Dr. Low [25] illustrating the changes of so-called toxic encephalitis. The differences from the extra-adventitial cell accumulations seen in postvaccinal encephalitis are only quantitative and may be due to the difference in the virulence of the toxin. In other words, the cause of postvaccinal encephalitis, as the histopathologic studies show, is not a dormant microbe aroused to life and action by vaccination, but most likely a toxin supplied by the vaccine lymph itself.

---

23. Hassin, G. B., and Diamond, I. Trichinosis Encephalitis, Arch. Neurol. & Psychiat. **15**:34 (Jan.) 1926.

24. Bailey, P.: Contribution to the Histopathology of Pseudotumor Cerebri, Arch. Neurol. & Psychiat. **4**:401 (Oct.) 1920.

25. Low, A. A.: Acute, Toxic (Nonsuppurative) Encephalitis in Children: A Clinicopathologic Study of Five Cases, Arch. Neurol. & Psychiat., to be published.

The mode of action of the toxin cannot be explained by histologic studies, nor can the latter explain why the complications should be prevalent in some countries, be ineffective in very young infants, become exceptionally virulent within a definite period of time and many other factors mentioned in this paper. In some cases of postvaccinal encephalitis it was noted that the scabs over the arms and the regional glands, when compared with those in a control case, showed the inflammatory reaction to be that of "vaccinia" of somewhat exceptional intensity" (Turnbull and McIntosh). This probably denotes that the virus contained in the lymph used in such cases was exceptionally strong and malignant.

For the foregoing reason it would seem logical that treatment should be prophylactic. It should be directed against flooding the body with toxins that may be present within the vaccine lymph. It is generally recommended to vaccinate as early in life as possible, and to use a vaccine that is as much diluted as possible. As Netter [26] put it, it is better to get an immunity which is less durable than to expose a person to grievous accidents and thus run a risk of discrediting so valuable a prophylactic remedy. One or two superficial insertions should suffice (Mader); in Holland, for instance, four insertions instead of five are recommended.[27] They should not be deep, and as little vaccine should be used as possible. In discussing postvaccination tetanus Armstrong [28] recommended that insertions should never be more than ⅛ inch (3.8 cm.) in their greatest diameter and preferably made by some method that does not remove the epidermis. He stated that the multiple pressure method advocated by Leake [29] is admirable. This method consists in making from twenty to thirty very superficial pricks of the skin through a drop of virus in an area not more than ⅛ inch in diameter. A sharp new needle is used. The virus is wiped off immediately. Hauswirth [30] insisted on a careful preliminary physical examination and on the postponement of vaccination if the child shows even the slightest indisposition. Yet, in spite of all possible precautions, complications could not be avoided (Bastiaanse's four cases, the case of Fulgham and Beykirch [31]).

---

26. Netter: Encephalitis postvaccinal, Bull. et mém. Soc. méd. d. hôp. de Paris **50**:1439, (Oct. 15) 1926.

27. Gildemeister, E.: Ueber Encephalitis post Vaccinationem, Centralbl. f. Bakteriol. **110**:120, 1929.

28. Armstrong, C.: Postvaccinal Tetanus and Its Prevention, J. A. M. A. **70**:738 (March 10) 1928.

29. Leake, J. P.: Pub. Health Rep. **42**:221 (Jan.) 1927.

30. Hauswirth, A.: Die stadtbernische Enquête der sogenannten Impfschäden anlässlich der obligatorischen Pockenschutzimpfungen, 1922-1924, Schweiz. med. Wchnschr. **56**:1113 (Nov. 20) 1926.

31. Fulgham, J., and Beykirch, J.: Postvaccinal Encephalitis, J. A. M. A. **92**: 1427 (April 27) 1929.

CONCLUSIONS

1. Vaccination against smallpox may cause cerebrospinal complications in the form of an acute nonpurulent encephalitis.

2. The encephalitis possesses typical pathologic features which may be termed cowpox encephalitis.

3. Cowpox encephalitis differs from epidemic (lethargic) encephalitis in its rapid course and in the absence of sequelae which are so typical of the latter.

4. Vaccination against smallpox should be preferably done in children less than 1 year of age with attenuated lymph and with as little trauma as possible.

5. Vaccination should be avoided in persons who are not altogether in good health, such as sufferers from tuberculosis or from an obscure febrile condition.

6. The exact cause of postvaccinal encephalitis is not known, but histologic studies show that the most probable cause is not an infection, but some toxin which is occasionally too virulent and is contained within the vaccine lymph.

HYPEROSTOSIS AND TUMOR INFILTRATION OF BASE OF SKULL ASSOCIATED WITH OVERLYING MENINGEAL FIBROBLASTOMA *

N. W. WINKELMAN, M.D.
PHILADELPHIA

Dr. William G. Spiller, in an article [1] entitled "Cranial Hyperostosis Associated with Underlying Meningeal Fibroblastoma," discussed the invasion of the bones of the skull over a fibroblastic tumor, the condition having been described by him originally in 1899. It is known that thickening of the bones of the vault is a not unusual accompaniment of an underlying fibroblastoma, and the appearance is characteristic in the x-ray film. Penfield, quoted by Spiller, stated that enlargement of the bones at the base of the skull from tumor infiltration in association with adjacent endothelioma would be of diagnostic importance in regard to the question of the origin of the bony enlargement. Spiller made the important observation that, as far as he knew, "in no case of fibroblastoma at the base of the skull has infiltration of the bone by the tumor been described." It was thought by both Spiller and Penfield that the finding of such infiltration of the bones at the base of the skull would throw much light on the still debated and extremely important question as to whether the bony thickening is the result of the tumor infiltration. Dr. Spiller was unable to refer to the paper by Kolodny,[2] which he considered of great importance, because it appeared after his own paper was in type.

When Dr. Spiller received the proofs of his article mentioned, I presented at one of our Saturday conferences the sections from a case of tumor of the frontal lobe with which there had been found associated a marked thickening of the roof of the ipsilateral orbit. As a result, Dr. Spiller appended a note to his paper giving me due credit for demonstrating for the first time invasion of the bone at the base of the skull by tumor cells of the same type as in an adjacent fibroblastoma. It is with the purpose of recording this observation that this report is made.

---

* Submitted for publication, July 10, 1929.

* From the Wards and Laboratory of Neuropathology of the Philadelphia General Hospital and the Graduate School of Medicine of the University of Pennsylvania.

1. Spiller, W. G.: Cranial Hyperostosis Associated with Underlying Meningeal Fibroblastomas, Arch. Neurol. & Psychiat. **21**:637 (March) 1929.

2. Kolodny, Anatole: Cranial Changes Associated with Meningioma, Surg. Gynec. Obst. **48**:231 (Feb.) 1929.

REPORT OF CASE

History.—A colored woman, aged 36, was first studied clinically and her condition diagnosed by Dr. J. W. McConnell; the case was reported by him from another angle as one of his many examples of tumors of the frontal lobe. Briefly, this history was as follows: In September, 1928, the patient noted dimness of vision, which was worse in the morning. About a month later, frontal headache began. When examined by Dr. McConnell she was loquacious, and showed

Fig. 1.—Floor of skull. Hemorrhagic staining, the result of operation, can be seen; also irregularity of roof of left orbit and anterior half of floor of middle fossa.

"Witzelsucht" and a tendency to yawn. There was incoordination of the right upper limb in the finger-to-nose test. The gait was not tested because the patient was too ill. All the reflexes were normal. At this time the right optic disk showed a choking of 5 diopters, while the left eyeground showed a condition "simulating albuminuric retinitis." The spinal pressure was 640 mm. of water. About a week after this examination, there was noted a definite weakness of the lower part of the right side of the face, as well as of the right upper limb. The diagnosis of a tumor of the left frontal lobe was made. An operation was refused.

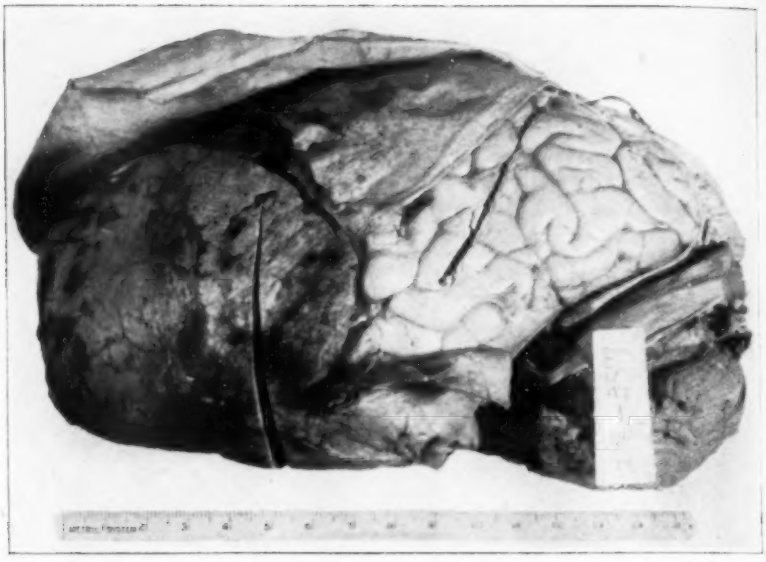


Fig. 2.—Lateral view of brain showing meningeal tumor covering the anterior half of left hemisphere.

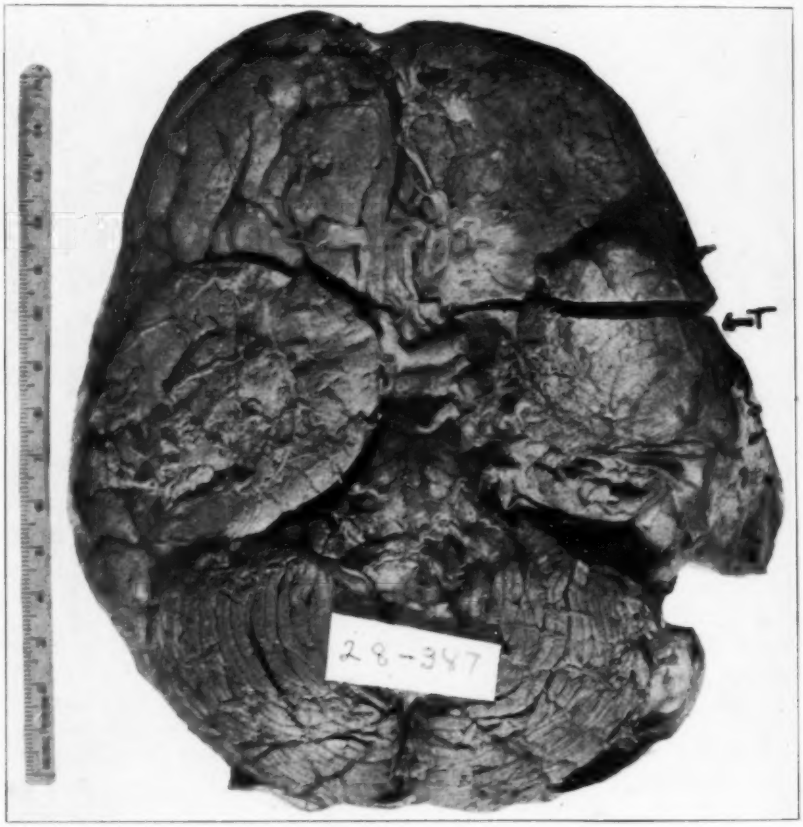


Fig. 3.—Inferior surface of brain showing covering of inferior surfaces of temporal and frontal areas by the tumor.

The patient was next seen at the Philadelphia General Hospital on Nov. 13, 1928, where the most prominent sign was great mental confusion. The neurologic signs were unaltered. The eyegrounds at this time showed a choking of 2.5 diopters in the right eye, with less swelling in the left eye. She was already blind and had secondary optic atrophy. Roentgen examination of the skull showed no

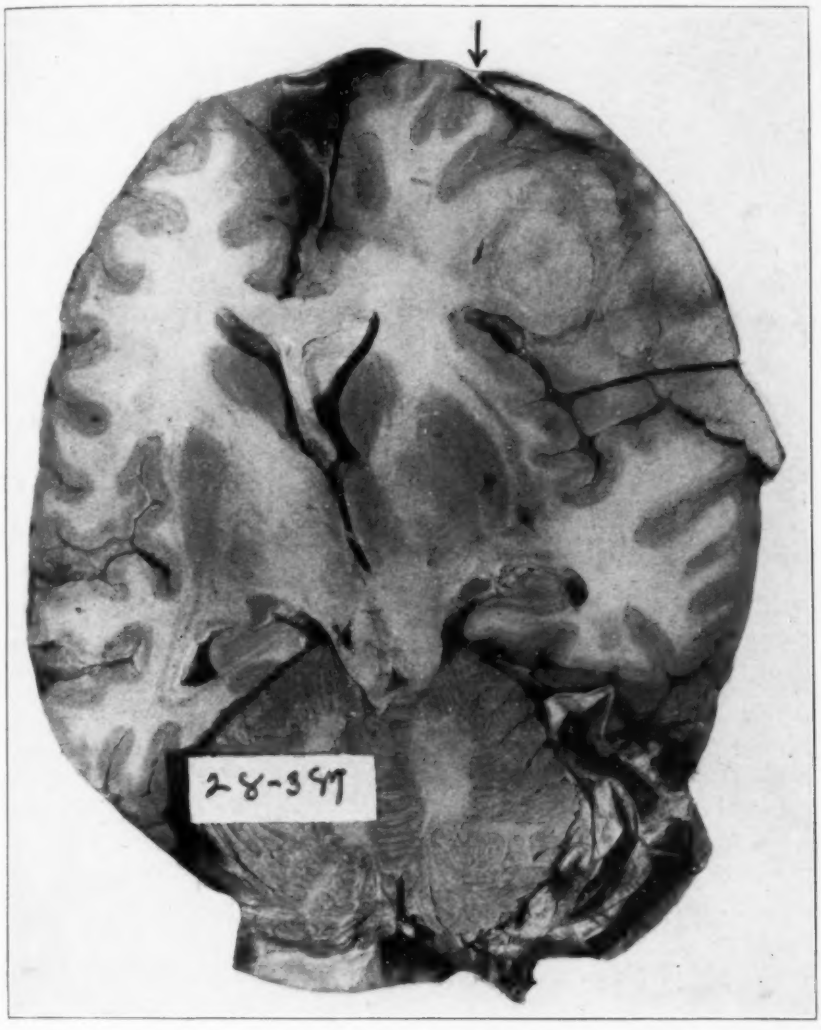


Fig. 4.—Low horizontal cut, showing the position of the tumor, compression of the anterior half of the brain and deviation of structures to the opposite side.

marked changes. An encephalogram was made but was unsatisfactory. A ventricular estimation and a left frontal exploration were then done, the surgeon discovering what appeared to be an enucleable tumor. Because of the condition of the patient no effort at removal was attempted. The patient did not survive the operation more than twenty-four hours.

Postmortem Examination.—After removal of the brain the skull was examined, and it was noted that the roof of the left orbit and the anterior portion of the floor of the middle fossa on the left side showed marked roughening (fig. 1). Both orbital roofs were removed for study and it was seen that the left was four or five times as thick as the right. Decalcification of both sides was done and a comparative study made.

The brain (figs. 2, 3 and 4) showed a tumor closely applied to and encircling the anterior part of the brain on the left side, going up on the lateral surface of the temporal, motor and frontal areas and covering the anterior part of the under surface of the temporal lobe and the posterior part of the orbital surface of the

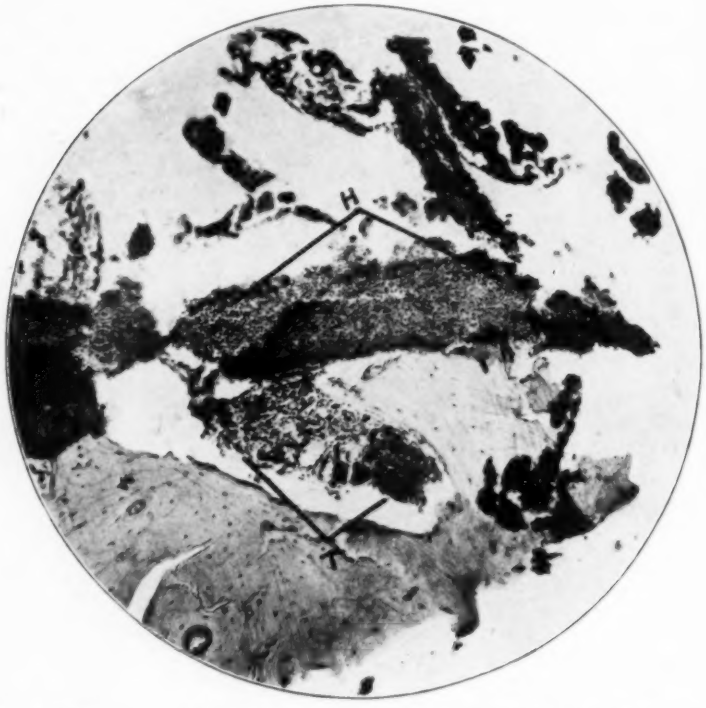


Fig. 5.—Microscopic picture of one of the two small islands of tumor tissue within marrow spaces (*T*). *H* indicates hemorrhage.

frontal lobe; it was so closely attached to the dura that it could not even be dissected away. The relative size of the tumor and brain can be seen from the illustrations.

Microscopic examination of the tumor mass showed a typical meningeal fibroblastoma without deep penetration into the dura. Microscopic examination of the bone of the left orbital roof showed definite thickening as compared with the normal side, but the bone itself was normal in every respect, with normal marrow in most of the spaces. In only two small marrow spaces was there any abnormality. Here one could see collections of cells that were foreign to the structure of the bone. They resembled morphologically in every way the tumor cells of

the overlying meningeal fibroblastoma. So small were these collections that diligent search was necessary before they were found (fig. 5). A considerable amount of congestion and hemorrhage can be seen.

COMMENT

This case is reported because it is the first one in the literature in which there has been found an invasion of the bones of the base of the skull by tumor cells from an adjacent meningeal fibroblastoma. Pancoast (quoted by Spiller [1]) has seen in the x-ray films in basal locations of this type of tumor, a diffuse bony thickening involving the squamous portion of the temporal bone, the great and lesser wings of the sphenoid, the orbital plate of the frontal bone, or all of these. According to Pancoast, the roentgen appearance changes from the radiating spicule type of the vertex to that of a dense thickening at the base. So that while increased density and thickening of bone does occur in association with meningeal tumors at the base, there has not been found infiltration of the bone by the tumor cells. The first explanation that would occur to one is that tumor infiltration has not been found in the bones at the base of the skull because these bones are rarely removed for histologic study. The fact that there is such a marked difference in the appearance shown in the roentgenogram, however, probably means that the condition itself is different. That tumor cells within the bones at the base of the skull are not common is attested by the fact that this is the first case in which I have found them in an intensive microscopic study of four cases.

This observation is of more than academic interest; it has several practical aspects. In the first place, it must be kept in mind by the surgeon in operating on tumors over the orbital plate, especially if thickening of the bone has been shown by the x-ray film. In the next place, it may help to throw light on the cause of bony thickening in association with meningeal fibroblastomas.

The important point that has been under discussion for many years as to the cause of the bony enlargement, or what has been called hemicraniosis, need only be touched on. Spiller has "not been convinced" that the cranial hyperostosis is always secondary to the meningeal growth as Cushing [3] has believed and taught; he has thought that trauma and syphilis may be important factors. Penfield (quoted by Spiller) has practically accepted the idea of Spiller that trauma is a likely causative factor for the hyperostosis. It is Cushing's belief, because endotheliomas tend to insinuate themselves into crevices and to surround blood vessels, that the tumor cells in the process of multiplication become crowded into and through the vascular dural spaces and finally into

3. Cushing, Harvey: The Cranial Hyperostoses Produced by Meningeal Endotheliomas, Arch. Neurol. & Psychiat. **8**:139 (Aug.) 1922.

the canaliculi of the bone. As a result the bone becomes irritated and subsequently osteoblastic proliferation occurs. Cushing admits that these tumors do not always behave alike in their effect on the bone. In some cases, aside from the increased vascularity with widening of the diploic venous channels due to stasis, there is no apparent change. This venous stasis may be an important factor, since von Recklinghausen [4] believed that new bone formation in ossifying carcinoma was due to the marked passive hyperemia produced.

The recent work of Kolodny [2] is extremely important and follows the line of thought of von Recklinghausen. Kolodny expressed the belief that the "proliferation of bone precedes the infiltration of the skull by tumor cells. This proliferation follows on the heel of a local dilatation of the vascular channels in the skull; it is probably the result of a defensive reaction of the bone to this slow, progressing dilatation of the blood vessels. Infiltration of the bone by tumor cells takes place subsequent to the commencement of the formation of new bone; it leads to bone destruction and occasionally to complete perforation of the skull."

Cranial hyperostosis of the vertex is not invariably present with underlying meningeal tumors (only in 20 per cent in Cushing's series [1]), but in "twenty or thirty" cases in which hyperostosis of the vault did occur Cushing found tumor cells present in every case. This has been my observation also in our series. Spiller,[1] however, has studied one case in whch no tumor cells were found after careful microscopic study. This I was able to verify through Dr. Spiller.

In the case reported in this paper, attention is called to the fact that while the bone was thickened to four or five times the size of that of the opposite side, it was only by the most careful search that two small nests of tumor cells, side by side, were located. Spiller's point I believe, is well taken when he said that the thickening of bone is out of proportion to the amount of tumor tissue present and "is evidence in this case that the thickening of bone was in no way the result of infiltration by tumor cells."

SUMMARY AND CONCLUSIONS

1. Tumor infiltration of the bone at the base of the skull in association with an overlying meningeal fibroblastoma is reported for the first time.

2. Attention is called to the great thickening of bone (from four to five times that of the opposite side) in contrast to the extremely small amount of tumor tissue present in the bone.

---

4. Von Recklinghausen, F. D.: Festschr. Rudolf Virchow, Berlin, 1891.

3. The outstanding theories as to the origin of the bony thickening are outlined: (*a*) Spiller's—that trauma and syphilis may play a part; (*b*) Cushing's—that the bony thickening is the result of tumor cell invasion of the bone; (*c*) Kolodny's—that the bony proliferation "follows on the heel of a local dilatation of the vascular channels in the skull," and that the infiltration of the tumor cells is subsequent to the commencement of the formation of new bone.

COCCIDIOIDAL GRANULOMA

REPORT OF TWO CASES SIMULATING TUMOR OF THE SPINAL CORD *

CARL W. RAND, M.D.
LOS ANGELES

Cases of coccidioidal granuloma are of increasing interest to those of us living in California. The disease was first described by Posadas [1] in Buenos Aires in 1900, the same case having been observed and reported independently by Wernicke [2] in 1892. Rixford,[3] in 1894, recognized the first case in California. This case with another observed by Thorne [4] was described later in greater detail by Rixford and Gilchrist,[5] who believed that the infecting organism was a protozoan belonging to the group of *Coccidia*, and suggested the name of *Coccidioides immitis* for the organism. Ophüls and Moffit,[6] in 1900, observed another case and found that the parasite grew readily on artificial mediums and developed a mold. It apparently belonged to the group of *Oidia*. Ophüls [7] then gave the name of *Oidium coccidioides* to the parasitic organism and coccidioidal granuloma to the lesion produced by it.

It is not the purpose of this report to describe the usual clinical picture with the various types of lesions which may appear in a patient suffering with a coccidioidal infection. Suffice it to say that the disease more closely resembles chronic tuberculosis than anything else, the two conditions being frequently confused. At this writing, approximately 98 cases of coccidioidal granuloma have been reported in the literature, while 143 have been reported to the California State Board of Health. The larger proportion of them have been found in California, and in

* Submitted for publication, June 10, 1929.

1. Posadas: Psorospermiose infectante généralisée, Rev. de chir. **21**:277, 1900.

2. Wernicke: Ueber einen Protozoanbefund bei Mycosis fungoides, Centralbl. f. Bakteriol. **12**:859, 1892.

3. Rixford: Case Demonstration, Occidental M. Times **8**:326, 1894.

4. Thorne, W. S.: A Case of Protozoic Skin Disease, Occidental M. Times **8**:704, 1894.

5. Rixford and Gilchrist: Two Cases of Protozoan (Coccidioidal) Infection of the Skin and Other Organs, Johns Hopkins Hosp. Rep. **1**:211, 1896.

6. Ophüls and Moffit: A New Pathogenic Mould, Phila. M. J. **5**:1471, 1900.

7. Ophüls, W.: Further Observations on a Pathogenic Mould Formerly Described as a Protozoan, J. Exper. Med. **6**:443, 1905.

these the majority of patients either have been residents of or have spent some time in the San Joaquin Valley. The primary lesion in the majority of cases is confined to the skin where nodular granulomatous areas, ultimately becoming ulcerated, occur. These ulcers may reach enormous proportions. Other cases present symptoms primarily of pulmonary infection, the lesion first appearing in the lungs and giving rise to a picture simulating tuberculosis. Again, the lesion may first appear in the joints, and in each case the bone and joint lesion is almost identical with the picture produced by tuberculosis of these structures. Practically all cases have been fatal, the disease running a course in time varying from a few months to several years. Tomlinson and Bancroft [8] emphasized the value of an intravenous injection of antimony and potassium tartrate, in addition to roentgenotherapy, and reported a case in which the condition was held in check tor two years by this treatment. Jacobson [9] placed considerable value on the use of colloidal copper in these cases. Dickson [10] said that, although the great majority of cases of coccidioidal granuloma prove fatal, "the progress of the disease may be prevented in a few cases by radical removal of the infected parts."

Occasionally, infection of the central nervous system has been observed. Ryfkogel,[11] in 1910, reported a case in a child which terminated with the symptoms of meningitis and in which treatment for cerebrospinal meningitis was instituted. Other cases have come to autopsy in which the meninges have been found infected with the *Oidium coccidioides*. Such cases have been reported by Dickson,[10] Ophüls [7] and others. Dickson likewise reported a case in which there was a general infection with *Oidium coccidioides*, the lumbar vertebrae being involved. He stated: "There was marked caseous destruction of the bodies of the vertebrae, and an abscess cavity extended along the course of the left iliopsoas muscle into the pelvis." Other cases of involvement of the bodies of various vertebrae have come to light, but they are rare. When these structures are infected, they take the form of a chronic process. So far as I can learn, no case of coccidoidal infection primarily involving the spinal cord or its coverings has heretofore been reported.

---

8. Tomlinson, C. C., and Bancroft, Paul: Granuloma Coccidioides, J. A. M. A. **91**:947 (Sept. 29) 1928.

9. Jacobson, H. P.: Coccidioidal Granuloma, California & West. Med. **29**:392, 1928.

10. Dickson, E. C.: Oidiomycosis in California, with Especial Reference to Coccidioidal Granuloma, Arch. Int. Med. **16**:1028 (Dec.) 1915.

11. Ryfkogel, H. A. L.: Coccidioidal Meningitis, J. A. M. A. **55**:1730 (Nov. 12) 1910.

REPORT OF CASES

CASE 1.—*Coccidioidal granuloma at level of sixth dorsal vertebra, simulating tumor of the spinal cord. Extradural granuloma penetrating the thoracic cavity removed at operation. Apparent recovery.*

History.—P. M., a Mexican woman, aged 31, married, a housewife, entered the Los Angeles General Hospital on Sept. 13, 1928, complaining of pain in the back and weakness of her legs. About five years previously, she had noticed pain in the left leg, which had recurred at intervals. About six months before examination, she had pain in the back which had continued. About five months before, she began to be weak on her feet, the gait became uncertain, staggering quickly developed, and the legs had gradually become weaker until she was paraplegic. She never had any cough or sign of pathologic involvement of the lungs, and the family history was negative for similar conditions. Through a social service worker it was learned that the patient with her family left Mexico in 1918, came to California and migrated to the following cities in the order named: Redlands, Santa Barbara, Fresno and Los Angeles. Fresno, as is well known, is in the heart of the San Joaquin Valley. They resided there for three years, beginning in 1920, and the patient worked in the vineyards picking grapes during the grape season. It would seem likely that she contracted the infection at this time.

Physical Examination.—Examination revealed an undernourished Mexican woman. The heart and lungs were clear. Roentgenograms of the chest showed the cardiac silhouette relatively normal in size and outline. Shadows of peribronchial structures were of average density and distribution. The parenchyma of both lungs was relatively clear. The observations were negative for evidence of a present active intrapulmonary pathologic process. There was no evidence of coccidioidal granuloma. The abdomen was normal save for a moderate fibroma of the uterus and a rectocele.

Examination of the Spinal Cord.—The patient was very spastic in both lower extremities. She was paraplegic and unable to walk even with assistance. There was considerable atrophy of both legs. She used the upper extremities normally.

There was complete loss of all forms of sensation ending abruptly at the ninth dorsal cord segment. Above this was a zone of hyperesthesia. Figure 1 illustrates the observations in a diagrammatic way.

The abdominal and epigastric reflexes were gone on both sides. The biceps, triceps, radial and finger jerks were active and equal. The knee jerks were tremendously exaggerated. The achilles jerks were quickened, the right being greater than the left. There was a double positive Babinski sign and a double positive ankle clonus.

There was incontinence of the urine, and bloating.

No trophic and vasomotor disturbance was noted.

Spinal fluid examination on Sept. 18, 1928, revealed a clear fluid under low pressure. This fluid contained 2 cells per cubic millimeter. The Wassermann test was negative, and Queckenstedt's test revealed a partial block. Five drops reduced Haines' solution in testing for sugar. The Wassermann reaction of the blood was negative. Urinalysis also gave negative results.

Roentgenograms of the dorsal and lumbar spines showed no pathologic process. There was tenderness over the seventh dorsal spine.

Diagnosis.—A diagnosis of tumor of the spinal cord at the ninth dorsal cord segment was made, and exploration was advised.

Operation.—On Oct. 4, 1928, a laminectomy was carried out in the middorsal region. The spines of the fifth, sixth and seventh dorsal vertebrae were removed with their laminae. The dura was uncovered. At the level of the fifth spine (sixth vertebra) an extradural, reddish-gray, soft, nonencapsulated tumor mass was found, firmly adherent to the dura at one point and having the gross appearance of a sarcoma. The mass was removed piecemeal, and frozen sections showed a coccidioidal granuloma. The mass extended around to the right side of the cord, going into the chest between the fifth and sixth ribs, where a pocket approximately 5 by 5 cm. in diameter filled with yellow caseous material was encountered and cleaned out by a curet. The mass in the chest seemed extrapleural. The dura was not opened. At the point of greatest dimension of the tumor in the spinal canal, the cord was greatly compressed. This compression was relieved by removal of the growth. The wound was closed tightly.

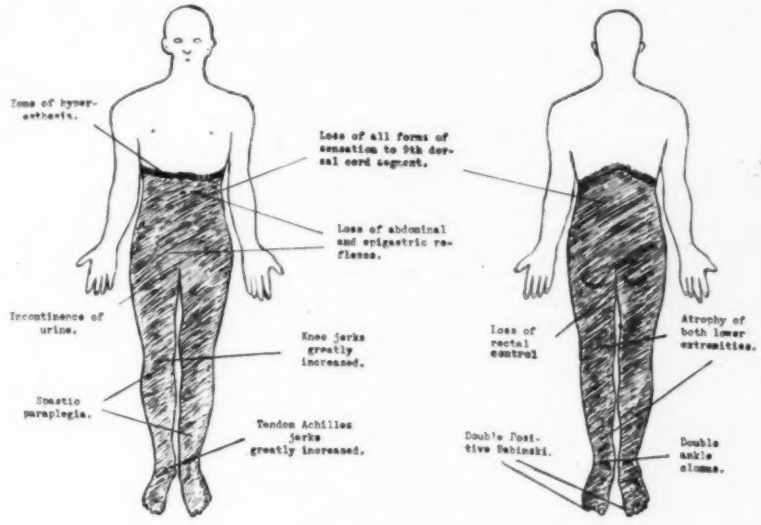

Zone of hyperesthesia.
Loss of all forms of sensation to 9th dorsal cord segment.
Loss of abdominal and epigastric reflexes.
Incontinence of urine.
Knee jerks greatly increased.
Spastic paraplegia.
Tendon Achilles jerks greatly increased.
Loss of rectal control
Atrophy of both lower extremities.
Double Positive Babinski.
Double ankle clonus.

Fig. 1 (case 1).—Diagrammatic representation of neurologic observations in case 1 before operation. These correspond almost identically with a tumor of the spinal cord at the ninth dorsal cord segment. Recovery followed operation.

Course.—It was expected that the tissues would break down, but this did not happen. The patient recovered completely from the paraplegia and left the hospital on Nov. 5, 1928; walking. She has remained well to date (although it is expected that there may be a recurrence) and at present is in good physical condition, doing her own housework and caring for three children.

Histologic Report: Dr. Newton Evans, pathologist for the hospital, gave the following report: The specimen consisted of about 5 Gm. of tissue fragments having a grayish-white, caseous appearance. Microscopic examination revealed the characteristic histologic structure of the lesions of coccidioidal granuloma, containing rather numerous parasites having the characteristic morphology of *Coccidioides immitis.* The microscopic structure of the granulomatous tissue in this case was similar to that described in other cases of this disease. It had a remarkable resemblance to tuberculous granulation tissue. There was much

dense scar tissue containing areas of round cells, most of which were of the plasma cell type. There were also present numbers of typical epithelioid cell tubercles containing large giant cells of the Langhans type, many of which contained the characteristic organisms (fig. 2). The organism was spherical, with a heavy hyaline capsule, and measured from 3 to 80 microns in diameter. In the tissue lesions it multiplied only by a type of sporulation, while in artificial culture it appeared as a mold, producing an abundant mycelial growth.

Fig. 2 (case 1).—Section of a giant cell taken from tissue in case 1; × 600. In the center one sees the organism of coccidioidal granuloma standing out. The individual spores are indistinctly seen but the double hyaline capsule presents a sharp contrast to the surrounding tissue.

CASE 2.—*Coccidioidal granuloma with the main lesion surrounding the cervical cord and smaller lesions scattered over or along the inferior surface of the cerebellum and pons. Early in its course, the condition resembled tuberculous meningitis; later, it resembled a tumor of the cervical cord. Death.*

History.—J. P., a Greek man, aged 38, married, a fruit dealer, was first seen in consultation with Dr. C. F. Nelson at the California Lutheran Hospital on

Feb. 16, 1929, when he was complaining of stiffness and soreness of the neck, headache, vomiting and beginning weakness of the arms. His father, mother, two sisters and two brothers were all living and well. There was no history of nervous diseases or tuberculosis in the family. He had never been subject to coughs or night sweats. A rectal fistula was operated on three years before. He had lived for nine years in the San Joaquin Valley, California, before coming to Los Angeles.

In August, 1928, he was taken ill with what was supposed to be pneumonia, was apparently very sick for a time and was confined to bed for about a month. Gradually the pneumonic process cleared up, but he did not recover strength. Early in October, he had a "fainting spell," apparently brought on by dizziness, and was unconscious for a short time. It is not known whether or not he had a convulsion at this time. About this time he began to complain of a tightening of the cords in the neck, and found that he could not bend the neck forward or turn the head freely because of stiffness and pain, which was particularly severe at the nape of the neck. He also began to complain of headaches. He was admitted to the St. Vincent's Hospital, Los Angeles, on Oct. 13, 1928, and discharged on Oct. 16, 1928. While there, he showed a slight stiffness of the neck, and the question of tuberculous meningitis was raised. A lumbar puncture was attempted, but no fluid was obtained. He left St. Vincent's Hospital and entered the Hollywood Hospital on Oct. 16, 1928, remaining until Nov. 29, 1928. While there, a presumptive diagnosis of tuberculous meningitis was again made. He had fever and chills and an almost continuous fever of from about 100 to 101 F., the temperature rising at about 8 o'clock each evening. He is also said to have had pleurisy and neuritis while there. The headache continued. There were stiffness of the neck and a persistent Kernig sign. The Wassermann reaction of the blood made at each of these hospitals was negative. The Widal reaction at St. Vincent's Hospital was suspicious. Hemoglobin was 80 per cent; red blood cells, 5,190,000; white blood cells, 10,812; lymphocytes, 23 per cent, and polymorphonuclears, 67 per cent.

During December, the condition grew worse. The patient was in bed most of the time. He was very weak and began to complain of pain in the limbs; a diagnosis of infectious arthritis was suggested. This was emphasized when several abscessed teeth were found and removed. He continued to have a low grade fever. On Jan. 4, 1929, a laparotomy was performed by Dr. Nelson and the appendix and gallbladder were removed. The symptoms were not improved by the laparatomy. He began to complain of more headache and at times would cough. A fluoroscopic examination of the lungs on Dec. 19, 1928, showed an old healed tuberculosis with much calcification involving both upper lobes of the lungs. Roentgenograms of the cervical spine taken on Dec. 7, 1928, showed no changes in the vertebrae, but marked calcification of both apexes of the lungs. Roentgenograms of the skull taken on Feb. 16, 1929, were normal, except for slight cloudiness of the left sphenoid.

During the early part of February, he began to show unmistakable signs of meningeal irritation. The headaches continued and at times were very severe, especially in the occipital and suboccipital regions; he began to vomit, this symptom becoming almost constant until his death, and he complained of pain in the back of the neck and stiffness of the neck. A double positive Kernig sign and a positive Brudzinski sign were elicited. On Feb. 4, 1929, a lumbar puncture was performed. The spinal fluid was found to be straw-colored but clear. It was under 200 mm. of pressure and contained 113 cells, most of which were polymorphonuclears. Globulin was greatly increased. The Wassermann reaction

was negative. The colloidal gold curve was 5555555533. A second spinal puncture was performed on Feb. 9, 1929, and again revealed a slightly straw-colored fluid which contained 122 cells per cubic millimeter. The globulin content was very much increased. The Wassermann reaction was again negative. The colloidal gold curve at this time was 5555555544. On Feb. 14, 1929, the hemoglobin was 85 per cent; color index, 0.93; red blood cells, 4,554,000; white blood cells, 5,900; polymorphonuclears, 67 per cent; lymphocytes, 31 per cent, and monocytes, 2 per cent. The nonprotein nitrogen of the blood was 31 mg. per hundred cubic centimeters; blood sugar, 91 mg.; chlorides, 462 mg. A urinalysis at this time gave negative results save for a faint trace of albumin and a few bacteria. The Wassermann reaction of the blood on Dec. 24, 1928, was negative. The temperature at this time was practically not above normal range, about 98 F.; the pulse rate was about 80, respiration rate 20, and blood pressure 120 systolic and 80 diastolic.

During February, 1929, the condition became worse. Pain in the occipital region increased, vomiting was almost continuous, mental confusion set in and the patient was restless and lethargic much of the time.

Examination.—At the time of my first examination, on Feb. 16, 1929, he showed definite stiffness of the neck, a positive Kernig sign on each side, and was rather inattentive to questions and examination. The cranial nerves were normal throughout. The eyegrounds were flat; the pupils were equal and reacted well. He showed considerable incoordination of both arms and legs which amounted to an ataxia. No sensory changes were made out, and he had control of the bladder and bowels. All deep reflexes were present and sluggish, but seemed equal on the two sides. No abnormal reflexes of the Babinski group were made out.

Course.—On the afternoon of February 16, he dropped into coma and remained unconscious for several hours. About this time he was examined by Dr. Thomas Orbison who found that there was positive ankle clonus on both sides, greater on the left than on the right, and the Babinski sign was positive on the right and negative on the left. The patient showed increased stiffness of the neck and an increased Kernig sign at this time. On Feb. 19, 1929, he was again unconscious for several hours, and the following day he developed weakness of the left hand which soon progressed to complete paralysis of this member. He also developed marked weakness of the right hand about this time. Sensory changes could be made out below the fifth cervical cord segment, but the patient did not cooperate well enough to be examined satisfactorily from this point of view. By Feb. 22, 1929, the paralysis had increased, both hands being completely paralyzed. He was able to flex the forearms on the arms but could not extend them; to raise the arms from the shoulders, but could not bring them down to the sides. The abdominal and epigastric reflexes were gone and other deep reflexes had completely disappeared. There was a suggestive Babinski sign on both sides. A fairly definite sensory level could be made out pointing practically to the fifth cervical cord segment (fig. 3). Breathing was becoming diaphragmatic. At this time, a diagnosis of a tumor of the spinal cord at about the fourth or fifth cervical cord segment was made. From this time on, the condition became worse, and he developed a complete flaccid quadriplegia with complete loss of all forms of sensation and complete disappearance of all superficial and deep reflexes. He was given subcutaneous injections of sterile dextrose until March 7, 1929, when he lapsed into coma and died.

Necropsy.—A postmortem examination of the brain and cord was made and revealed a coccidioidal granuloma of the cervical cord. The granuloma was sub-

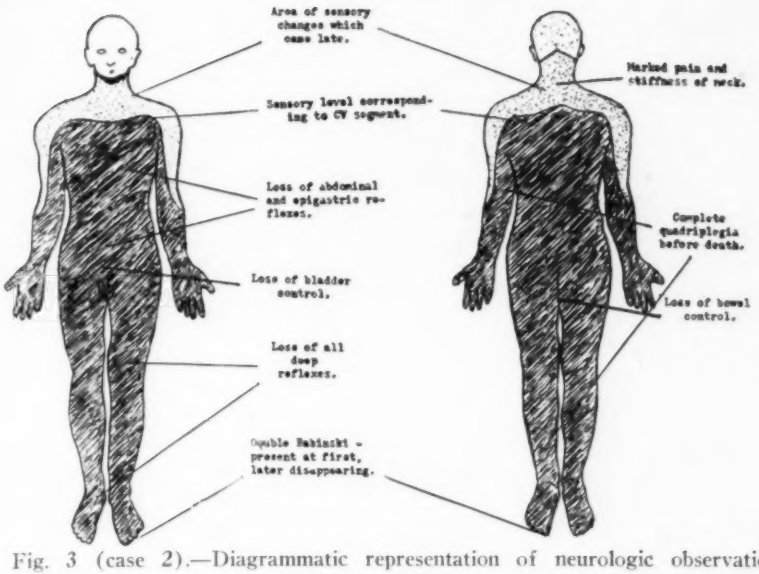

Area of sensory changes which came late.
Marked pain and stiffness of neck.
Sensory level corresponding to CV segment.
Loss of abdominal and epigastric reflexes.
Complete quadriplegia before death.
Loss of bladder control.
Loss of bowel control.
Loss of all deep reflexes.
Double Babinski - present at first, later disappearing.

Fig. 3 (case 2).—Diagrammatic representation of neurologic observations shortly before death. An extensive coccidioidal granuloma was found surrounding the cervical cord at autopsy. The inferior surface of the cerebellum and pons as well as the region of the sylvian fissures showed patches of meningitis, but the syndrome of a high cervical cord lesion was the predominating picture.

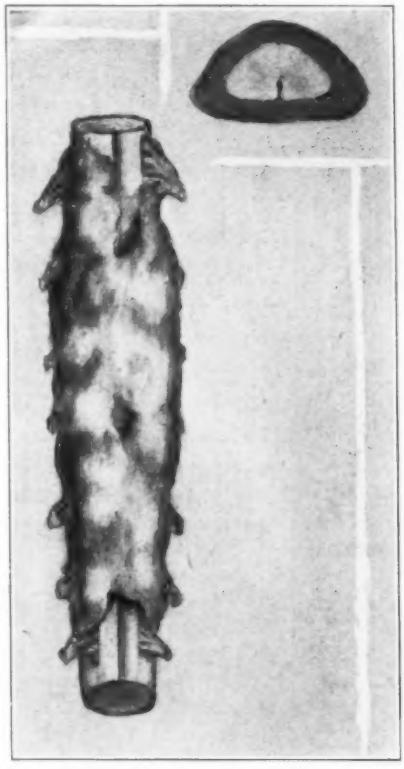


Fig. 4 (case 2).—Schematic reconstruction of coccidioidal granulomatous tissue surrounding the cervical cord. This tissue wrapped itself about the cord in the subdural space like a cuff, but did not penetrate the substance of the cervical cord itself; it apparently extended from below upward, producing a clinical picture of an ascending cervical compression.

dural and completely surrounded the cord like a cuff (fig. 4). It apparently grew upward, thus accounting for the gradually ascending clinical symptoms. A microscopic study showed a typical picture of coccidioidal granuloma. Figure 5 shows microscopically how the granulation tissue wrapped itself about the cervical cord.

Dr. George Maner, the pathologist, gave the following report: The brain and an attached 6 inch segment of the spinal cord were examined. The cerebral hemispheres were symmetrical. The pia-arachnoid over the vertex was edematous. In the pia of both sylvian fissures there were numerous small pearly gray miliary nodules resembling tubercles. There was thick, tough, yellowish-gray

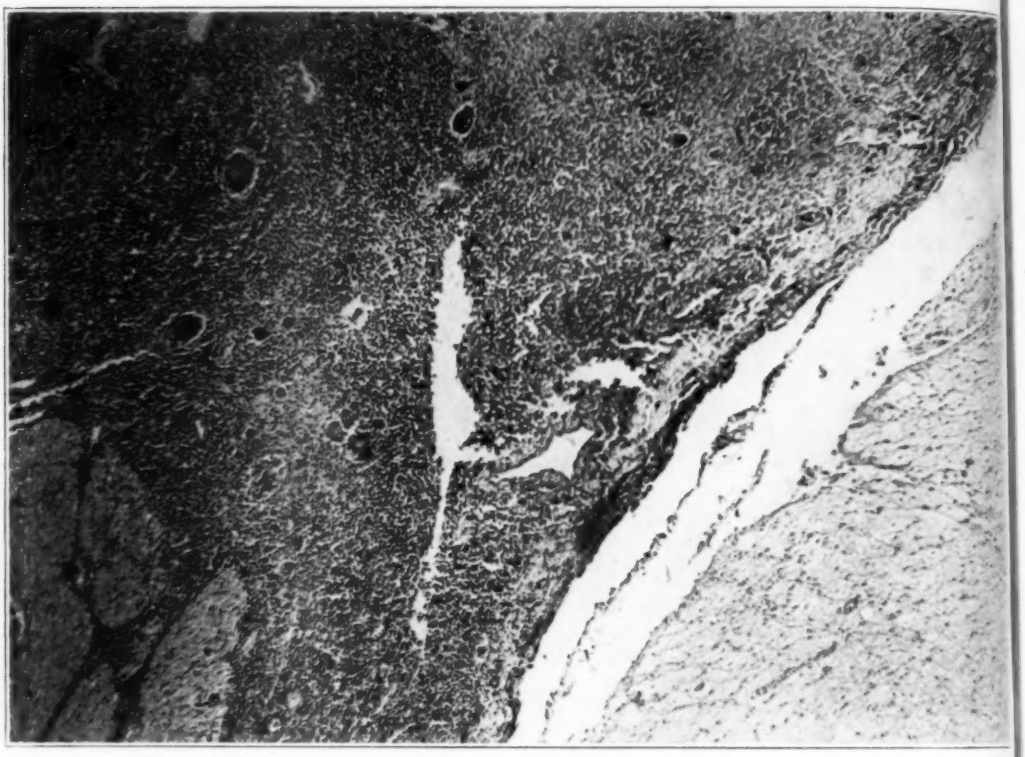


Fig. 5 (case 2).—Low power magnification of cervical cord and surrounding coccidioidal granuloma; × 70. Many giant cells can be seen scattered throughout the granulation tissue. A nerve root is seen in the lower left hand corner and a section of the spinal cord in the lower right hand corner. Between the granulation tissue and the spinal cord one makes out a thin strip of tissue suggestive of the arachnoid or pia. The dura lies outside the granulation tissue and is not seen in this section.

exudate on the inferior surface just posterior to the optic chiasm and over the pons. The inferior surface of the cerebellum was covered with exudate. Sections in the transverse plane showed no tumors, abscesses or hemorrhages.

The spinal cord was completely encircled in a coat-sleeve fashion by exudate; this was especially thick, about 0.25 cm., at the level of the third and fourth

cervical segments. The exudate was yellowish-gray and tough. Sections through the cord at various levels showed no apparent gross change.

Microscopic examination revealed that the pia in the sylvian fissures was thickened and contained many circumscribed collections of epithelioid and lymphoid cells with small foci of central necrosis and accumulations of polymorphonuclear leukocytes. Some of these nodules contained large multinucleated Langhans' giant cells with one or more double contoured spheroidal organisms resembling *Coccidioides immitis*. Many of these organisms contained endospores. There were a few giant cells and organisms scattered throughout the exudate. There were many mononuclear wandering cells of the plasma and lymphoid cell variety.

The exudate around the cord was considerably thicker and was within the pia. The giant cells were more numerous and contained more sporulating organisms, as many as seven being seen in one cell. There was no apparent involvement of the cord.

Diagnosis: Coccidioidal meningitis involving the cervical cord, inferior surface of the cerebellum and pons and sylvian fissures was present.

SUMMARY AND CONCLUSIONS

Two cases of coccidioidal granuloma involving the central nervous system, clinically resembling tumors of the spinal cord, are presented. In case 1 the picture was that of compression of the cord at the ninth dorsal segment. At operation an extradural coccidioidal granulomatous mass was encountered and removed, with relief from symptoms. There has been no recurrence eight months later. In case 2 the early symptoms pointed to meningeal irritation or inflammation, a diagnosis of tuberculous meningitis having been made by several observers. As the disease progressed, increasing evidence of compression of the cervical cord appeared. At the time of my first observation the patient had a lesion corresponding to the level of the fifth cervical cord segment. Within a short time this had ascended to the region of the first cervical cord segment, causing death by respiratory failure. Both instances showed so great a resemblance to tumor of the spinal cord that exploration was advised. In the first case it was carried out and proved beneficial; in the second it was refused and subsequent events proved that, in fact, an inoperable condition existed.

The great similarity between coccidioidal infections and chronic tuberculosis has been described repeatedly by practically all writers on the subject. In view of this fact and in consideration also of the pathologic process detailed in the cases reported here, it might not be amiss to liken the observed condition to the tuberculoma of the spinal cord occasionally seen in chronic tuberculosis. When localizing symptoms of spinal cord compression appear, an exploratory laminectomy seems justified.

PARALYTIC DEMENTIA

THE LOCALIZATION OF SPIROCHAETA PALLIDA IN THE BRAIN *

CHARLES G. AARS, M.D.
Formerly Assistant Dermatologist, University of Leyden, Holland
PARAMARIBO, DUTCH GUIANA

In a recent study of the brain in thirteen cases of paresis and in three cases of cerebral syphilis I found *Spirochaeta pallida* in nine cases of the former disease. The tissues had been fixed in formaldehyde, and some of the brains had remained in this solution for years. The Jahnel method,[1] slightly modified, was used and in most cases seventeen regions of the brain were examined: gyrus rectus, gyrus frontalis inferior, gyrus frontalis superior, gyrus temporalis superior, gyrus temporalis inferior, gyrus centralis anterior, gyrus centralis posterior, cornu ammonis, lobus parietalis, gyrus occipitalis, thalamus, insula, medulla oblongata, pons varolii, substantia nigra, corpus striatum and cerebellum.

Spirochetes were found in nearly all the regions named; I did not find them in the medulla oblongata, pons varolii or cerebellum, though they have been observed in these regions,[2] nor did I observe them in the meninges as reported by Jahnel, Carp and others.

The anamneses in these cases were typical for paresis; Nissl preparations were used for histopathologic diagnosis. When differential diagnosis was difficult, I used also the Spatz carbon bisulphide reaction.

Some of the results of my studies of these brains have already been recorded.[3] Here I propose to record observations concerning the localization of the spirochetes.

---

* Submitted for publication, March 15, 1929.

1. Jahnel, F.: Studien über die progressive Paralyse, Arch. f. Psychiat. **57**: 382 and 847, 1917; Ein Verfahren zur elektiven Spirochaetendarstellung in einzelnen Schnitten des Zentralnervensystems, Deutsche med. Wchnschr. **29**:793, 1920.

2. Jahnel, F.: Ueber das Vorkommen von Spirochäten im Kleinhirn bei der progressiven Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **36**:335, 1917; Die Spirochäten im Zentralnervensystem bei der Paralyse, ibid. **73**:310, 1917. Carp, E. A. D. E.: Over de Localisatie der Spirochaeta Pallida in de Hersenen bij Progressieve Paralyse, Nederl. Tijdschr. v. Geneesk. **71**:386, 1927.

3. Aars, C. G.: Het Treponema Pallidum in de Hersenen bij Dementia Paralytica, Leiden, S. C. van Doesburgh, 1928, p. 93; Het Treponema Pallidum in de Hersenen bij Dementia Paralytica, Nederl. Maandschr. v. Geneesk. **15**:129 (March) 1928.

GENERAL LOCALIZATION

It may be stated, in general, that the greatest number of spirochetes are localized in the anterior part of the cerebrum. One finds them in all the layers of Brodmann; the medulla cerebri contains very few of them. Though it has been stated by some observers that the lamina zonalis does not contain parasites, many others have found them there. Noguchi failed to find the spirochetes in that layer and found most of them in Brodmann's layers 2 to 6. Marinesco and Minea also found them mostly in the lamina pyramidalis and deeper layers, as did Raecke.[4]

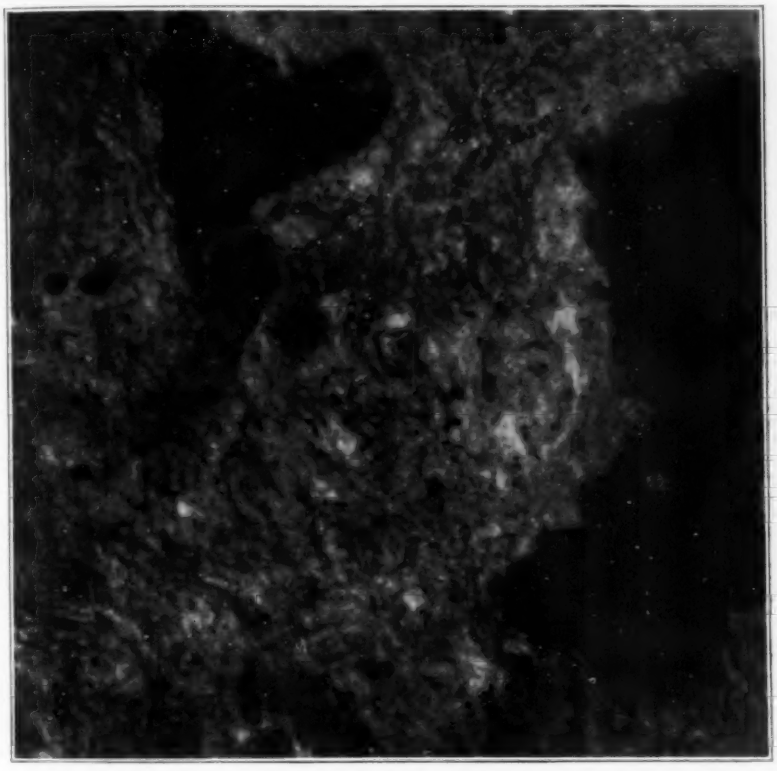


Fig. 1.—Substantia nigra. Spirochaeta pallida lying near a large pigment cell; it has probably wandered into the brain tissue from the capillary.

Jahnel[5] gave the following localization: As a rule the spirochetes are limited to the second, third, fourth, fifth and sixth layers, while they are rarely present in the lamina zonalis. At the junction of the marrow and cortex the dense mass of parasites, as can be seen in some cases,

4. Raecke, J.: Die Bedeutung der Spirochätenbefunde im Gehirn von Paralytiken, Arch. f. Psychiat. **57**:593, 1917.

5. Jahnel, F.: Ueber die Lokalisation der Spirochäten im Gehirn bei der progressiven Paralyse, Neurol. Centralbl. **36**:402 (May) 1917.

is sharply demarcated; they are absent in the medulla, or only a few of them can be detected there. In the second layer Jahnel saw his so-called "Einrollungsformen," parasites with one or two rolled-up ends, sometimes forming a ring. Jahnel seldom found spirochetes in the lamina zonalis.

Carp and I came to the same conclusions concerning the quantitative distribution of the spirochetes in the different layers of the brain. Most of the spirochetes were observed in the deeper layers of the cortex (fourth, fifth and sixth). A considerable number of parasites were present in the lamina pyramidalis, while only seldom did the two superficial layers contain spirochetes.

LOCALIZATION OF THE SPIROCHETES WITH REGARD TO THE BLOOD VESSELS

As Schaudinn declared, one must consider the syphilitic roseola as an embolism of the capillaries of the papillae of the cutis with spirochetes. He was able to demonstrate them there without difficulty. Seldom, however, could they be demonstrated inside the vessels of the brain. Only a few authors claim to have seen spirochetes in these blood vessels. The facts concerning this will probably always remain questionable, for many so-called intravascular localizations may prove to be only an optical illusion when studied with the eyes of a critical microscopist.

In most cases, the spirochetes are localized just over or beneath a blood vessel or they are situated in its walls. Artificially, the parasites can obtain an intravascular localization, if by section of the blocks they have been swept into the lumen from the walls. A beautiful photograph in the publication of Carp shows a "true" intravascular localization. Here one sees a spirochete joining itself closely to a red blood corpuscle. Versé [6] was able to demonstrate the same condition in a case of phlebitis luetica cerebrospinalis; here spirochetes were seen joining themselves to chromocytes and endothelial cells. This condition has also been observed by Ranke in a case of lues cerebri congenita. The surrounding tissue did not show spirochetes in this case.

Raecke, Jahnel, Hauptmann,[7] McIntosh and Fildes, Hermel,[8] Schob [9] and others never observed an intravascular localization. Still the picture

6. Versé, M.: Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie, Ziegler's Beiträge z. path. Anat., 1913, vol. 56.

7. Hauptmann, A.: Spirochaeten und Hirnrindengefässe bei Paralyze, Ztschr. f. d. ges. Neurol. u. Psychiat. **57**:122, 1920.

8. Hermel, H.: Ueber Spirochaetenbefunde bei atypischen Paralysen, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:417, 1921.

9. Schob, F.: Ueber miliare Nekrosen und Abscesse in der Hirnrinde eines Paralytikers und ihre Beziehungen zur Spirochaeta pallida, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:588, 1925.

was often suggestive. On the other hand, Levaditi, Marie and Bankowsky, Sioli,[10] and Pacheco e Silva [11] are convinced of the existence of intravascular localization. The last named writer expressed his belief that the spirochetes are most numerous at the bifurcations of the capillaries and explained this by the very slow flow of the blood in these places. On only one occasion did Jahnel discover a spirochete inside a blood vessel; he never saw this again. He stated his belief that this condition is caused by a postmortem process.

Fig. 2.—The spirochetes appear to be lying inside the vessel. On focusing with the micrometer head, one sees that the parasites are localized in the wall of the vessel or around it.

It is surprising that while the spirochetes can only rarely be demonstrated in the lumen they are often present in the walls of the brain vessels. Sometimes these walls appear black with spirochetes; in most cases the organisms lie lengthways, in others they are localized trans-

10. Sioli, F.: Die Spirochaeta pallida bei der progressiven Paralyse, Arch. f. Psychiat. **60**:401, 1919.

11. Pacheco e Silva, A. C.: Localisation du tréponème pallidum dans le cerveau des paralytiques généraux: considérations thérapeutiques, Rev. neurol. **33**:558 (June) 1926.

versely to the vessels. Here one must consider two possibilities: They can penetrate into the walls from the lumen, or they attack the walls from the surrounding tissue.

When one finds a large number of parasites in the walls they may have multiplied there or have invaded the walls "en masse." Sometimes one sees only involvement of the walls, while the surrounding tissue is relatively free from the organisms. In such cases one can observe complexes of transverse sections of small vessels, the walls of which

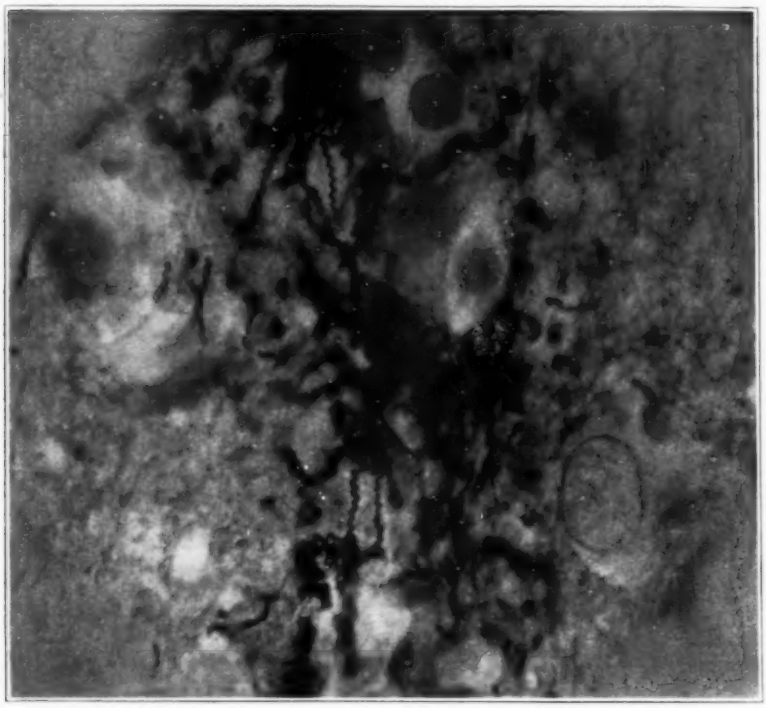


Fig. 3.—The environment of the blood vessel is practically free from spirochetes.

are black with spirochetes. Probably Hauptmann [12] was right when he considered that these small vessels belong to a larger, primarily involved vessel, in the wall of which a multiplication of the spirochetes has occurred. In this way the parasites could follow the smaller vessels for some distance. On the other hand, in some cases there can be seen large groups of small vessels and capillaries free from spirochetes, while

12. Hauptmann, A.: Spirochäten und Hirnrindengefässe bei Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **57**:122, 1920.

the organisms form a dense mass around the glia perivascularis. There are also parts where the parasites lie diffusely in the tissue without penetrating into the vessel walls. Here one can think that the new growth of capillaries occurred after the invasion of the tissue by the spirochetes.

LOCALIZATION OF THE SPIROCHETES WITH REGARD TO CELLS

Often large numbers of parasites can be seen around the ganglion cells; an intracellular localization proved to be very rare. Noguchi described the relation of the spirochetes to the ectodermal cells of the brain. His silver preparations were stained with toluidine blue. By this method he observed often that one or more parasites were lying close to a pyramidal cell, and that in some cases part of the spirochetes seemed to be inserted in the cytoplasm of the nerve cell. These nerve cells showed distinct signs of degeneration: irregular forms, swelling or incomplete lysis of the nucleus.

Marinesco and Minea, who published their observations in one positive case in a study of the brain of twenty-seven paretic persons, concluded that only seldom do the spirochetes show some relation to the vessels, the ganglion and the glia cells. They believed, however, that they had seen parasites in some ganglion cells.

Raecke spoke of "umzingeln, durchdringen" and "zerfressen von" ganglion cells by the spirochetes. He found them intracellularly beside the nucleus or covering the nucleus like a cap; a parasite was seen even inside a nucleus. From these observations he considered that the degeneration of the nerve cells is caused by mechanical factors. On the other hand, Jahnel [13] declared that intracellular localization or nerve cell penetration occurs very rarely.

The spirochetes were observed by Sioli and Hauptmann inside the glia cells. In most cases, however, the organisms did not show a tendency to penetrate into them.

Involvement of ganglion cells by the spirochetes was never seen by Hauptmann and Cappola. Schob, Manuélian and Bertollucci are convinced of the existence of endocellular localization. This is not the opinion of Pacheco e Silva, who declared:

". . . Nous sommes absolument sûrs, étant données les nombreuses préparations que nous avons examinées, que la tréponème ne pénètre pas à l'intérieur de la cellule nerveuse, qui, au lieu de lui servir d'abri, est au contraire une barrière à l'invasion tréponémique." (We are absolutely certain, on the basis of our

13. Jahnel, F.: Ueber einige Beziehungen der Spirochäten zu dem paralytischen Krankheitsvorgang, Ztschr. f. d. ges. Neurol. u. Psychiat. **42**:21, 1918.

study of many specimens that the treponema does not penetrate the interior of the nerve cells, which do not serve as a shelter, but on the contrary act as a barrier to invasion by the spirochete.)

My own observations are negative concerning the intracellular localization in nerve cells. After impregnation the preparations were stained with toluidine blue. Notwithstanding this, the parasites could easily be detected; the nerve cells proved to have suffered badly from the silver method. On account of my observations I cannot agree with Raecke, who believed in mechanical damaging of the nerve cells by the penetrating parasites. I could never see the organisms attached or joined to these cells. Like most other investigators I am inclined to think that the ganglion cells die, intoxicated by endotoxins or exotoxins of the surrounding wall of spirochetes. Autointoxication of the starving cell, because the parasites are robbing the cell of essential food, is another possibility. In most cases even the neighborhood of the ganglion cells was free from the organisms and it is striking that so many of these cells show little or no alteration. From this one may conclude that the sensitive nerve cell is damaged by the spirochetes only with difficulty or slowly.

As regards the relation of the spirochetes to the mesodermal cells, parasites have been seen in plasma cells by Marcus [14] and Sioli. However, the sketches given by the former are not convincing and have been criticized by many authors. Schob also claimed to have seen the spirochetes in white blood cells. In his publication one sees sketches of multiple abscesses of the brain, which he thinks are of spirochetal origin. The leukocytes contain all sorts of clumps and other impregnated corpuscles. It is to be regretted that he did not publish photographs. The clinical symptoms and pathologic changes in this case justified the diagnosis of paresis. Raecke said: "In der Regel war mit Bestimmtheit jede nähere Beziehung zwischen Spirochäten and Exsudatzellen auszuschliessen." (As a rule, it was possible definitely to exclude any close relationship between spirochetes and exudate cells.) He believed that the presence of a large number of spirochetes prevents the formation of an infiltration and that on the other hand no parasites will be found in places where large plasma cell infiltrations are present. Hauptmann, Jahnel, Valente and others never saw intracellular involvement of leukocytes. Jahnel and Raecke observed the organisms inside a rod cell. In my cases there was not one preparation in which I could observe an intracellular localization of the parasites, in cells either of mesodermal or of ectodermal origin.

---

14. Marcus, H.: Spirochaeta pallida in den Plasmazellen bei der progressiven Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **26**:245, 1914.

THERAPEUTIC SUGGESTIONS

In contemplating the preparations one comes to the following question: Do these studies bring a solution of the therapeutic problem of paresis?

Perhaps they may in the future, but at this moment one can only say that there are hopeful points and that parasitologic study of the brain in cases of paresis is needed. Using this method one can decide what are the results of chemotherapy as well as of other sorts of treatment (malaria, recurrent fever and other artificially caused infections).

Two of the sixteen patients in the cases studied had been treated by malarial inoculation. These brains showed no spirochetes, which is in accordance with the observations of Freeman [15] and others. Two other patients with negative parasitologic observations had been treated intensively with neoarsphenamine (intravenous and intralumbar injections). These were the only four patients who had received antisyphilitic treatment during the stage of paresis. Naturally, I do not pretend that all such cases would prove free from spirochetes (in the brain), but this fact suggests careful investigation of more paretic brains. It has never been proved that arsphenamine preparations do not penetrate into the parenchymatous tissue. Perhaps this kind of investigation would throw light on this point.

As a result of my studies I agree with Hoche [16] and others that, parasitologically, paresis begins long before the clinical diagnosis is made. Treatment for syphilis in the earlier stages should be most carefully given and it is a pity that one is not able to give all patients regular courses of treatment, more or less as Fournier indicated years ago. None of my sixteen patients had been treated at all or they had received insufficient treatment before the outbreak of paresis. The results of experimental studies (on chemotherapy of animals inoculated with *Spirillum recurrens*) are still contradictory (Kolle, Prigge,[17] Buschke and others) and I think that there is as yet no indication for changing the therapy.

CONCLUSIONS

1. The Jahnel method is the best impregnation procedure for detecting *Spirochaeta pallida* in brains of paretic patients.

2. The spirochetes can be observed in all layers of the cortex cerebri.

---

15. Freeman, W.: Treatment of General Paralysis: Histopathologic Observations in Fifteen Cases, J. A. M. A. **88**:1064 (April 2) 1927.

16. Hoche, A.: Die Heilbarkeit der progressiven Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **43**:430, 1918.

17. Prigge, R.: Die Sterilisierung mit Salvarsan und die Beziehungen der Immunität zur Persistenz der Spirochäten bei experimenteller Recurrensinfektion der Mäuse, Dermat. Ztschr. **47**:1, 1926.

3. Spirochetes could be found in nearly all regions of the brain.

4. Intravascular and intracellular localization of *Spirochaeta pallida* in the brain has been reported. From the study in my cases I believe that this is very rare. I never saw these conditions.

5. The microscopic-parasitologic study of paretic brains is useful for answering the question whether arsphenamine preparations penetrate into the parenchymatous tissue.

6. Studies of the literature and my own investigations lead me to advocate strongly the regular treatment for syphilis in the early stages, with the hope of preventing the development of paresis.

STUDIES IN EPILEPSY

IX. THE SUGAR CONTENT OF THE SPINAL FLUID*

WILLIAM G. LENNOX, M.D.
AND
MARGARET B. ALLEN, B.S.
BOSTON

The oxidation of dextrose is an important element in the nutrition of nerve, as well as of other, cells. The occurrence of nervous symptoms, which sometimes include convulsions, is a striking accompaniment of hypoglycemic reactions. Irritability of nerves has been shown to increase along with a decrease of blood sugar. For these reasons, it is important that all phases of carbohydrate metabolism should be studied in persons who are subject to seizures. We have already discussed this question and have presented data concerning blood sugar and blood sugar curves in large numbers of epileptic patients.[1] In spite of individual variations from normal, the evidence gathered indicates that the sugar of the blood plays but a passive rôle in epileptic seizures.

It is possible, however, that there might be abnormalities in the sugar content of tissues other than the blood; the spinal fluid, for example. Such abnormalities of the spinal fluid have been demonstrated in various diseases of the central nervous system. In order to determine whether the occurrence of convulsions had any relationship to such changes, we measured the sugar in the spinal fluid of a number of epileptic patients. The scattered references in the literature have been reviewed by Lennox and Cobb.[2] The only adequate series of cases studied from this standpoint is that by Osnato and Killian,[3] who found normal values in sixty-nine institutionalized epileptic patients.

* Submitted for publication, Sept. 10, 1929.

* From the Department of Neuropathology, Harvard Medical School, and the Thorndike Memorial Laboratory, Boston City Hospital.

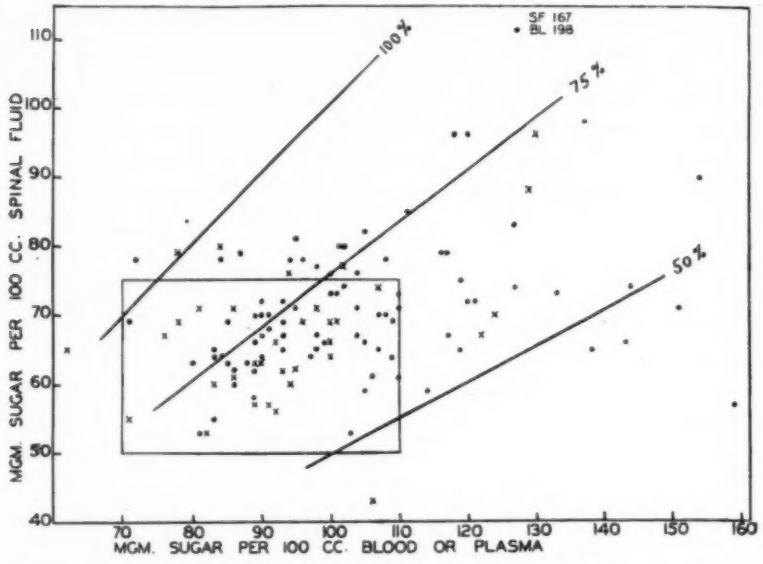
1. Lennox, W. G.; O'Connor, M., and Bellinger, M.: Studies of Metabolism in Epilepsy: II. The Sugar Content of the Blood, Arch. Neurol. & Psychiat. **18**:383 (Sept.) 1927. Lennox, W. G., and Bellinger, M.: Studies of Metabolism in Epilepsy: III. The Blood Sugar Curve, Arch. Neurol. & Psychiat. **18**:395 (Sept.) 1927.

2. Lennox and Cobb: Epilepsy, Baltimore, Williams & Wilkins Company, 1928.

3. Osnato, M., and Killian, J. A.: Biochemical Studies of the Blood and Spinal Fluid in Epilepsy, Brain **50**:581, 1927.

MATERIAL AND METHODS

Our subjects were either private patients or those being treated by the neurologic staff of the Boston City Hospital. Lumbar puncture of patients having seizures was done as a routine procedure, so that the present group was unselected. Both sexes and all ages, above childhood, were represented. Only one patient, who had a blood sugar of 198 mg., was diabetic. Venous blood was drawn after the lumbar puncture was completed. Analysis of the sugar was made by the method of Folin-Wu,[4] the sugar tubes of Evans and Rothberg[5] being used.



Measurement of sugar in the blood and spinal fluid. The ordinates represent measurements for spinal fluid, the abscissae those for blood or plasma. Determinations for whole blood are shown by dots and for plasma by crosses. The rectangle represents the limits of normal for fasting persons. The diagonal lines indicate measurements of sugar in the spinal fluid which are, respectively, 100, 75 and 50 per cent those of the blood or plasma.

RESULTS

Results of measurements in 113 patients are shown in the accompanying chart. In this chart the values found in the spinal fluid and in the blood, for each patient, are plotted against each other and are

4. Folin, O., and Wu, H.: A System of Blood Analysis, J. Biol. Chem. **41**:467 (March) 1920.

5. Evans, F. A., and Rothberg, V. E.: A Modified Folin and Wu Blood Sugar Method, J. Biol. Chem. **58**:443, 1923.

represented by a single dot. If blood plasma, rather than whole blood, was used, the measurement is represented by a cross. The rectangle represents the limits usually accepted for normal fasting persons—from 70 to 110 mg. per hundred cubic centimeters of blood or plasma and from 50 to 75 mg. per hundred cubic centimeters of spinal fluid.[6] The diagonal lines indicate measurements of sugar in the spinal fluid which are, respectively, 100, 75 and 50 per cent those of blood.

It was not feasible to secure all of the specimens at a time when the patients had been without food for twelve hours or longer; therefore, our values cannot be expected to fall within the strict normal limits marked by the rectangles. Of the 113 measurements, in only two instances was the concentration of sugar in either the blood or the spinal fluid below normal. Twenty-seven of the blood measurements and twenty-eight of the spinal fluid measurements were above normal, although in only eleven patients were the values for both blood and spinal fluid high. Of those patients whose blood sugar value was below 110 mg. only seventeen had a spinal fluid value above 75 and one a value below 50 mg.

Because of the disturbing factor of food, we were more interested in the ratio between the blood and the spinal fluid sugar than in their absolute values. In normal fasting persons, the concentration of sugar in the spinal fluid is ordinarily from 50 to 75 per cent that in the blood. It will be seen that our values show a wider scattering, though all but eight are between the limits of 50 and 100 per cent. The variations observed could be accounted for by the fact that some patients had taken food several hours before the punctures were made. In such patients with falling blood sugar, we should have the condition noted in the upper left portion of the chart, in which values in the blood were rather low and those in the spinal fluid relatively and absolutely high. In securing simultaneous curves for the sugar of the blood and spinal fluid, Fremont-Smith [6] observed that the spinal fluid curve lagged behind the blood sugar curve, so that, with persons whose blood sugar had been high for some time and had then fallen rapidly, the concentration in the spinal fluid might exceed that in the blood.

It will be noted that in our series the ratio of spinal fluid to blood sugar varied for different levels of blood sugar. Thus, of thirty-four patients whose blood sugar was below 90 mg. per hundred cubic centimeters, fourteen (41 per cent) showed a spinal fluid-blood sugar ratio

6. Fremont-Smith, F., and Dailey, M. E.: The Normal and Abnormal Quantitative Sugar Content: The Human Cerebrospinal Fluid, New York, Paul B. Hoeber, Inc., 1926, p. 104.

below 75 per cent. On the other hand, of seventeen patients with blood sugar above 120 mg., fifteen (88 per cent) showed a ratio below 75 per cent. This is undoubtedly a normal condition, representing the slow changes that occur in the composition of the spinal fluid reservoir in contrast with the swift changes that occur in the blood river.

SUMMARY

In 113 patients with epilepsy the sugar content of the spinal fluid, with respect to that of the blood, was normal.

STUDIES IN EPILEPSY

X. THE CHLORIDE CONTENT OF THE BLOOD AND SPINAL FLUID*

WILLIAM G. LENNOX, M.D.
AND
MARGARET B. ALLEN, B.S.
BOSTON

It has long been stated that in epilepsy the chlorides in the body bear a relationship to seizures. In the arguments concerning this theory, chloride has been considered in two aspects: (1) as a conductor of electricity and (2) in its other physicochemical relations.

The first conception is largely speculative. The steps in the argument, baldly expressed, are somewhat as follows: Nerve cells are storage batteries. Convulsions result from an explosive discharge of these cell batteries. Such a discharge and the subsequent passage of the nervous impulse are facilitated if the salt content of the tissues is high. The principal salt of the body is sodium chloride; therefore, in epileptic patients the accumulation of chloride in the tissues and particularly in the brain may result in seizures. This analogy of the cortical motor cells to an electric storage battery that periodically "builds up" and discharges is used to explain the relative immunity to attacks which often follows a severe seizure. Flesch [1] has elaborated this theory. Crile [2] has measured the differences in electric potential of various tissues of the body with reference to stimulation of the suprarenal and thyroid glands. He stated that the salt content of the tissues influences such changes in potential. Such arguments as applied to epilepsy are as yet too nearly metaphysical to be convincing.

Somewhat more familiar ground is a consideration of changes in the physiology and chemistry of nervous tissue as related to chloride metabolism. Increase in the concentration of chloride in the brain results in edema (Haldi, Rauth, Larkins and Wright [3]), and cerebral edema in itself may cause convulsions. Again, the chlorides comprise

* Submitted for publication, Oct. 14, 1929.

* From the Department of Neuropathology, Harvard Medical School and the Thorndike Memorial Laboratory, Boston City Hospital.

1. Flesch, J.: Epilepsiestudien, Neurol. Centralbl. **36**:434 (June 1) 1917.

2. Crile, G. W.: New Clinical and Experimental Studies of Interrelations of Thyroid, Adrenals and Nervous System, New England J. Med. **198**:988 (June 28) 1928.

3. Haldi, J. A.; Rauth, J. W.; Larkins, J., and Wright, P.: A Study of Anion and Cation Effects on Water Absorption by Brain Tissue, Am. J. Physiol. **80**:631 (May) 1927.

two thirds of the acid bodies contained in normal blood plasma, and the rapid exchange of chloride from cells to plasma and from blood to body tissues is an important means by which the neutrality of the body fluids is regulated. In epilepsy there is a definite relationship between acid-base changes and seizures, a condition of alkalosis tending to increase and acidosis tending to decrease attacks. One might reason that an increase in chloride, an acid substance, should be of benefit in epilepsy. However, as we shall describe later, such an increase may be accompanied by a proportionate increase in base, so that the acid-base equilibrium is not disturbed. Indeed, the three conditions of increased concentration of chlorides, acidity and edema are so intimately related that it is difficult to separate one from the other and say, "This is the factor of basic importance."

In attempting to evaluate the influence of chlorides in epilepsy, we first wish to know whether alteration of the salt intake in patients has any effect on seizures. Many physicians, especially in Europe, have made it a practice to limit the ingestion of sodium chloride. The largest experience is that of Ulrich.[4] The benefit from such limitations is presumed to be due to the replacement of chloride by bromide, which is given at the same time, but it is possible that the reduction of chloride in itself is of some significance. Reduction of sodium chloride intake alone, without the use of bromide, is a common practice with many physicians, but reports of the results obtained have been too few to permit conclusions. Sherrill[5] obtained no benefit in five patients. Freudenberg,[6] and Vollmer and Serebrijski,[7] each of whom alternately fed and withheld salt from a single patient, concluded that increased chloride in the blood was accompanied by seizures. In the experiments quoted, fluid balance was not measured, and therefore nothing could be said as to whether the changes in the water content or in the chloride content of tissues were more important. In conditions of fasting there is, of course, salt starvation and some reduction in the level of chlorides in the blood. It would seem probable, however, that the beneficial effect of fasting is due to the resulting acidosis rather than to reduction in the concentration of salt. In our experience, feeding sodium chloride during fasting has not resulted in a return of seizures. In

4. Ulrich, A.: The Bromide-Chloride Treatment of Epilepsy, M. J. & Rec. **126**:41 (July 6) 1927; 88 (July 20) 1927; 156 (Aug. 3) 1927; 245 (Aug. 17) 1927.

5. Sherrill, J. W.: Metabolic Observations on Psychiatric Cases, J. Metab. Research **5**:129 (Jan.-March) 1924.

6. Freudenberg, E.: Beitrag zur Epilepsiebehandlung, Ztschr. f. Kinderh. **41**:46, 1926.

7. Vollmer, H., and Serebrijski, J.: Epilepsiestoffwechsel, Ztschr. f. Kinderh. **41**:314 (June) 1926.

such cases, a correlating curve representing the daily number of seizures will not parallel the level of chloride in the plasma or the water balance as nearly as it will parallel the concentration of plasma bicarbonate. One such experiment is shown in figures 11 and 12 in the book on epilepsy by Lennox and Cobb.[8]

As has been stated, the question of the chloride content of the tissues is intimately related to that of the acid-base equilibrium, so that one must know whether the chloride is all covered by a base or is partly free. If a neutral salt such as sodium chloride is ingested there will be little or no change in the acid-base equilibrium. If, on the other hand, an acid-forming salt, such as calcium chloride, is taken, only the chloride is retained in the body and a condition of uncompensated acidosis results. Though the effect of feeding sodium chloride has not been adequately studied, the evidence at hand points toward an increase in seizures with its use. If, on the contrary, an acid-forming salt is fed, there is a temporary decrease in seizures paralleling the decrease in plasma bicarbonate and running counter to the increase in plasma chloride (figure 10, Lennox and Cobb[8]). This experience has been confirmed by Dennig,[9] but not by Peterman.[10] Continued use of one of these acid-forming salts in our patients has ended in marked epileptic manifestations, the suggestion being that eventually the accumulation of chlorides has had an untoward effect, overmatching the initial benefit of the acidosis.

These clinical considerations make measurements of chloride in the body fluids of considerable interest. The measurements of blood chlorides reported by Weston,[11] Pezzali,[12] Sherrill,[5] Freudenberg,[6] Vollmer and Serebrijski,[7] because they dealt with ten patients or fewer, are without much value. Weeks, Allen, Renner and Wishart[13] found rather low values in forty-three patients examined. These patients, however, had been on a diet low in salt.

Our chief interest lies in the tissues rather than in the blood. One must remember that there may be considerable alteration in the salt content of tissues without parallel changes in the blood. Important information may be gained through measurement of the chloride bal-

8. Lennox, W. G., and Cobb, S.: Epilepsy, Baltimore, Williams & Wilkins Company, 1928.

9. Dennig, H.: Deutsche Ztschr. f. Nervenh. **103**:275, 1928.

10. Peterman, M. G.: The Ketogenic Diet, J. A. M. A. **90**:1427 (May 5) 1928.

11. Weston, P. G.: Analyses of Blood of Insane Patients, Arch. Neurol. & Psychiat. **3**:147 (Feb.) 1920.

12. Pezzali, G.: Ricerche sul contenuto del sangue in azoto (residuo), cloruri, calesterina, grassi, glucosi, indicano e calcio nell'epilessia, Riforma med. **39**:433 (May 7) 1923.

13. Weeks, D. F.; Allen, F. M.; Renner, D. S., and Wishart, M. B.: Fasting and Diets in Treatment of Epilepsy, J. Metab. Research **3**:317 (Feb.) 1923.

ance of the body. In one experiment performed with an epileptic child, Gamble and Hamilton [14] found that in spite of a measured chloride intake and a constant, carefully balanced diet there was a marked fluctuation in chloride excretion from day to day, the excess excretion occurring on days when the child had seizures. Since the blood chlorides remained fairly constant, there must have been considerable change in the tissue chlorides with relation to seizures. More such carefully controlled observations are needed.

No means of directly estimating the chloride content of tissues are available. It is probable, however, that the chemical composition of spinal fluid is representative of that of fluid contained in body tissues. Therefore, coincident analyses of chloride in the blood and spinal fluid may throw light on the relative concentration of chlorides in blood and in body water. Such measurements made by Hamilton [15] in seventeen cases of epilepsy were reported as normal.

MATERIAL AND METHODS

The patients whom we examined were being treated in the neurologic department of the Boston City Hospital. They were of various ages and of both sexes. They were patients having seizures as a presenting symptom. No attempt was made to select those having so-called essential epilepsy. In most instances blood and spinal fluid were drawn without reference to the ingestion of food. Food intake makes little difference in the level of chloride in the blood. Blood for examination was drawn at the conclusion of the lumbar puncture. Patients were not on a limited salt intake. The method of Whitehorn [16] was used for measurement of chlorides. As indicated in the chart, in some instances whole blood, and in other instances blood plasma, was used.

RESULTS

One hundred and twenty patients were examined. The measurements obtained are shown graphically in the accompanying chart. In this chart each dot or cross represents the measurement of the chloride in both the spinal fluid and the blood in each patient. The small rectangles show the strict limits for normal persons as given by Fremont-Smith and Dailey [17] and by Myers.[18] The diagonal lines represent the ratio of the concentration of chloride in the spinal fluid to the concentration in the blood.

---

14. Gamble, J. L., and Hamilton, B.: The Acid-Base Composition of Urine from an Epileptic, Bull. Johns Hopkins Hosp. **41**:389 (Dec.) 1927.

15. Hamilton, B.: Comparison of Concentrations of Inorganic Substances in Serum and Spinal Fluid, J. Biol. Chem. **65**:101 (Aug.) 1925.

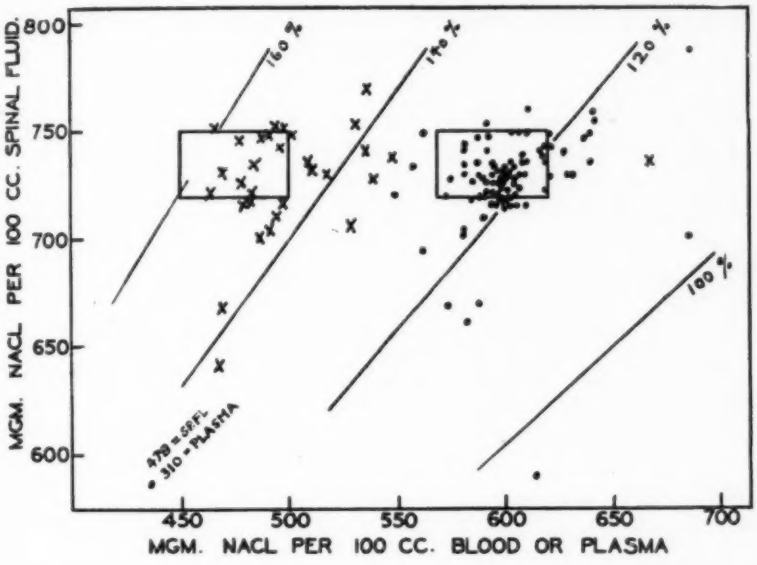
16. Whitehorn, J. C.: Simplified Method for the Determination of Chlorides in Blood or Plasma, J. Biol. Chem. **45**:449, 1921.

17. Fremont-Smith, F., and Dailey, M. E.: Cerebrospinal Fluid Chlorides, Arch. Neurol. & Psychiat. **14**:509 (Oct.) 1925.

18. Myers, V. C.: Chemical Changes in Blood in Disease, J. Lab. & Clin. Med. **5**:343, 1920.

Concerning the values of chloride found in the blood and plasma, it will be seen that of the 120 patients, only 4 had a concentration lower than normal, whereas 21, or 18 per cent, had values above normal. Therefore, 79 per cent of the total number of patients showed normal blood values. As regards the measurements of the spinal fluid, 10 were above and 25 below normal, that is, 71 per cent were normal. This is a slightly larger scattering than was present in the blood. Except for a few instances, the variations from normal were not great.

We are principally interested in the question as to whether the ratio between chlorides in blood and spinal fluid is normal. Ordinarily the concentration in the spinal fluid is considerably higher than that in the



Measurements of sodium chloride in spinal fluid and in whole blood or plasma. The ordinate represents concentration in the spinal fluid; the abscissa that in plasma (represented by dots) and in whole blood (represented by crosses). Each dot or cross gives the measurement for chloride in both the spinal fluid and the blood. The small rectangles represent strict limits of normal, the left for whole blood, the right for plasma. The diagonal lines show various proportions of chloride present in the spinal fluid with reference to that in the blood.

blood because of the low protein content of the spinal fluid. If one accepts as normal the ratio of chlorides for the two fluids as shown within the rectangles in the chart, one would expect the chloride of spinal fluid to be about 150 per cent that of whole blood and about 125 per cent that of plasma. Inspection of the chart shows that in the epileptic patients the ratios are somewhat lower than this, the average being about 145 per cent for blood and 120 per cent for plasma. The

latter ratio is about the same as the ratio between the chloride content of plasma and that of whole blood. If the chloride in the spinal fluid increased proportionately with that in the blood, one would expect the dots or crosses to be arranged parallel to the diagonal lines. There is no great tendency in this direction.

From the previous discussion, one would expect that if epileptic patients showed abnormality in the spinal fluid-blood chloride ratio, it would be in the direction of a relatively high value in the spinal fluid. The slight average variation from normal present was in the opposite direction. Though many of our patients have an increase in the total protein of the spinal fluid, the increase was not great enough to account for the observed decrease in spinal fluid chlorides.

On the whole, though there were individual unexplained variations from normal, the average measurements in both blood and spinal fluid were essentially normal. Although such a normal condition is present in these patients, it is possible and even probable that marked variations in the chloride content of blood or of tissues may have a precipitating or an inhibiting effect on seizures. If this is true, the situation as regards chlorides would be analogous to the situation found for the acid-base relationships. Although any marked abnormality in the acid-base equilibrium in epileptic patients has not been demonstrated, an upset in the existing equilibrium tends to increase or decrease seizures. In the same way, although epileptic patients show a normal condition as regards chloride metabolism, it would seem probable that an increase of chlorides in tissues tends to induce seizures. This question, however, needs further careful study.

SUMMARY AND CONCLUSION

Simultaneous measurements were made of the chloride in the blood and in the spinal fluid in 120 patients subject to epilepsy. The average value for chloride in the blood and in the spinal fluid and the ratio of chloride in the spinal fluid to that in the blood were within the limits of normal.

THE KAHN PRESUMPTIVE PROCEDURE WITH SPINAL FLUIDS*

ELIZABETH B. McDERMOTT
ANN ARBOR, MICH.

Kahn has recently published a highly sensitive method with spinal fluids for detecting neurosyphilitic involvement, known as the presumptive procedure.[1] A similar method with serum has already been in use for several years supplementary to the regular Kahn test with serum, which is conservative in sensitiveness.[2] Many reports have appeared in the literature on the regular test with spinal fluid, the consensus being that this test is specific for neurosyphilis but is conservative in sensitiveness.[3] A highly sensitive method with spinal fluids would be of great value to clinicians, since it might detect invasion of the central nervous system by *Spirochaeta pallida* before the appearance of clinical symptoms. In this article, I shall discuss the relative increase in sensitiveness of the presumptive procedure over the regular Kahn test with spinal fluids.

In July, 1928, the Kahn test was made standard in the serologic laboratory of the University of Michigan Hospital. Each specimen of blood and spinal fluid received in the laboratory is tested by the regular and the presumptive procedures. An opportunity was thus offered to study the degree of increased sensitiveness of the presumptive procedure over the regular test. Altogether, 1,358 examinations were made with both methods, and the cases included different pathologic conditions other than syphilis, as well as the cases of untreated and treated patients with syphilis.

TECHNIC

The technic of the presumptive procedure is similar to that of the regular test, except that "sensitized" antigen is employed instead of "standard" antigen. Briefly it is as follows: The spinal fluid specimen, after being freed from foreign

* Submitted for publication, June 17, 1929.

* From the Serological Laboratory, University Hospital, University of Michigan.

1. Kahn, R. L.: The Kahn Test: A Practical Guide, Baltimore, Williams & Wilkins Company, 1928, p. 166.

2. Kahn (footnote 1, p. 152).

3. Keim, H. L., and Kahn, R. L.: Clinical Studies on the Kahn Reaction for Syphilis: III. The Test with Spinal Fluids, J. A. M. A. **84**:881 (March 21) 1925. Lederer, A.: Quantitative Kahn Test, Procedure for Spinal Fluids, U. S. Vet. Bur. Med. Bull. **3**:52, 1927. Hull, T. G.; Fry, L., and Garwood, C.: The Kahn Test on Spinal Fluid, Am. J. Syph. **12**:104, 1928. Rabinovitch, A., and Roberts, C.: A Comparative Study of the Kahn and Complement Fixation Tests of Spinal Fluid, U. S. Vet. Bur. Med. Bull. **4**:692, 1928.

material by means of centrifugation, is measured in an amount of 1.5 cc. into a small test tube. To the same tube is added 1.5 cc. of a saturated solution of ammonium sulphate of high purity. After the contents are mixed thoroughly, the tube is placed in a water bath at 56 C. for fifteen minutes—to insure complete precipitation of the globulins. The tube is then centrifugated and the supernatant fluid removed from the globulin precipitate. To the precipitate is added 0.15 cc. of physiologic solution of sodium chloride, i. e., one tenth of the original amount of spinal fluid, in which the globulin is dissolved. This concentrated solution of globulin is then ready to be tested with antigen suspension. "Sensitized" Kahn antigen is mixed with salt solution in accordance with the titer. After it has stood for ten minutes, 0.01 cc. of the antigen suspension is measured into the bottom of a small test tube with a 0.2 cc. pipet graduated in 0.001 cc. Into the same tube is then measured 0.15 cc. of the globulin solution. The mixture is shaken for three minutes at a speed of from 275 to 285 oscillations per minute

TABLE 1.—*Increase in Sensitiveness of Presumptive Procedure Over Regular Kahn Test with 1,358 Spinal Fluids*

Reactions Obtained with Presumptive Procedure		Regular Test	
624	++++ or +++ *	462	++++ or +++
		35	++ or +
		24	±
		103	0
43	++ or +	6	±
		37	0
41	±	41	0
650	0	4	++ or +
		1	±
		645	0

Total Reactions and Percentage

	++++ or +++	Per Cent	++ or +	Per Cent	±	Per Cent	0	Per Cent
Presumptive procedure	624	45.9	43	3.1	41	3.0	650	47.8
Regular test	462	34.0	39	2.8	31	2.2	826	60.7

* ++++ or +++ indicates strong precipitation; ++ or +, moderate precipitation; ±, weak or borderline precipitation; 0, no precipitation.

and 0.5 cc. of salt solution is added. The reaction is now completed. A strong precipitate is read ++++; weaker precipitates are read +++, ++, +, ± and — respectively. A ++++ or +++ reaction is reported as positive, ++ or + weakly positive and ± or — as negative.

RESULTS

Increase in Sensitiveness of Presumptive Procedure over Regular Test in General Hospital Cases.—Table 1 summarizes the increase in sensitiveness of the presumptive procedure over the regular test in the 1,358 examinations of spinal fluid. Of 624 fluids which gave ++++ or +++ reactions with the presumptive procedure, 462 gave similar reactions, 35 ++ or +, 24 ± and 103 negative reactions with the regular test. Of 43 fluids which were ++ or + with the presumptive procedure, 6 were ± and 37 negative with the regular test. Forty-one fluids which showed a ± reaction with the presumptive procedure

were negative with the regular test. Of 650 fluids that were negative with the more sensitive procedure, 4 were ++ or +, 1 was ± and 645 were negative with the regular test.

In considering the increase in sensitiveness of the presumptive procedure over the regular test on a percentage basis, it is found that the former method gave 45.9 per cent ++++ or +++ reactions against 34 per cent with the regular test. In the case of ++ or + reactions, the increase in sensitiveness was only 0.2 per cent, while in the case of ± reactions, the increase was 0.8 per cent.

Increase in Sensitiveness of Presumptive Procedure over Regular Test in Treated Patients with Syphilis.—The degree of increased sensitiveness of the presumptive procedure was also determined in a group

TABLE 2.—*Increase in Sensitiveness of Presumptive Kahn Procedure Over Regular Test with 150 Spinal Fluids from Treated Patients*

Reactions Obtained with Presumptive Procedure		Regular Test	
102	++++ or +++ *	80	++++ or +++
		6	++ or +
		4	±
		12	0
11	++ or +	2	±
		9	0
37	0	37	0

	Total Reactions and Percentage					
	++++ or +++	Per Cent	++ or +	Per Cent	0	Per Cent
Presumptive procedure	102	68.0	11	7.3	37	24.6
Regular test	80	53.3	6	4.0	58	38.6

* ++++ or +++ indicates strong precipitation; ++ or +, moderate precipitation; ±, weak or borderline precipitation; 0, no precipitation.

of patients undergoing antisyphilitic therapy. Table 2 summarizes the results of 150 examinations with the presumptive and regular tests. It is seen from this table that of 102 ++++ or +++ reactions with the more sensitive procedure, 80 gave similar reactions, 6 ++ or +, 4 ± and 12 negative reactions with the regular test. Of 11 ++ or+ reactions with the presumptive procedure, 2 were ± and 9 were negative with the regular test. Thirty-seven fluids reacted negatively with both methods. On a percentage basis, the presumptive procedure gave 68 per cent of ++++ or +++ reactions against 53.3 per cent with the regular test. In the case of ++ or + reactions, the presumptive gave 7.3 per cent against 4 per cent of reactions with the regular test.

COMMENT

It is evident from the results presented that the presumptive procedure with spinal fluids is markedly more sensitive than the regular test with these fluids. The latter test has proved to be of approximately

the same degree of sensitiveness as dependable Wassermann tests. This fact is illustrated by the observations of a number of workers,[3] and especially by the recent "competition" of the regular Kahn and Wassermann tests with spinal fluids carried out in London under the auspices of the League of Nations Health Committee.[4] Of 555 spinal fluids examined with both methods, the Kahn test gave 241 positive reactions against 240 similar reactions given by the Wassermann test. Consequently, there is a corresponding increase in sensitiveness of the presumptive procedure over different Wassermann tests as over the regular Kahn test. It is apparent, therefore, that the presumptive procedure represents the most sensitive method available today for the detection of neurosyphilis.

With regard to specificity of this procedure, preliminary studies indicate that positive reactions are occasionally obtained in cases free from clinical manifestations of neurosyphilis. These reactions, however, in my studies so far have proved to be from cases of syphilis. Considering this fact, it seems possible that the positive presumptive reaction is an indicator of early invasion of the organisms before sufficient injury has been done to give clinical manifestations. It is hoped that different workers will study the significance of the positive presumptive reactions in the face of negative reactions with the regular test and in the absence of clinical manifestations.

The value of the presumptive procedure lies in the fact that it is a check on the regular spinal fluid test, two methods being obviously more dependable than one. Due to the increased sensitiveness, it strengthens the diagnostic significance of the weak or borderline reactions of the regular test. Negative presumptive reactions, furthermore, are obviously stronger indicators of the absence of neurosyphilis than similar reactions with the regular test. In addition, positive presumptive reactions against negative reactions with the regular test, and in the apparent absence of clinical neurosyphilitic manifestations, should serve as a stimulus to clinicians to search thoroughly for such manifestations for an extended period of time.

SUMMARY

A comparison was made of the sensitiveness of the regular and presumptive Kahn procedures with spinal fluids, based on 1,358 examinations. It was found that in the general run of hospital cases the presumptive procedure was 12 per cent more sensitive than the regular test, and in a group of 150 treated patients with syphilis, the presumptive procedure was 18 per cent more sensitive.

4. League of Nations Health Committee Report of Conference on Serodiagnosis of Syphilis, Copenhagen, 1928, Geneva.

The presumptive procedure appears to be the most sensitive serologic method available for detecting neurosyphilis and is of special value as a supplementary method to the regular Kahn test with spinal fluid. The negative reactions of the presumptive procedure should aid in eliminating neurosyphilitic involvement, and the positive reactions against negative results with the regular Kahn test should serve as a stimulus in searching for neurosyphilitic manifestations in syphilitic patients.

Clinical Notes

BROWN-SÉQUARD SYNDROME AS A MANIFESTATION OF SYPHILITIC NEURORECURRENCE

Report of a Case *

JUI-WU MU, M.D., AND CHESTER N. FRAZIER, M.D.
PEIPING, CHINA

Although syphilis, according to Oppenheim [1] and others, is not infrequently responsible for the causation of the Brown-Séquard syndrome, we have been able to find no instance on record in which the syndrome has been the manifestation of syphilitic neurorecurrence involving the spinal meninges—that is to say, the manifestation of an acute syphilitic meningitis following the lapse of treatment with arsphenamine in a case of early syphilis which originally had no clinical or serologic signs of involvement of the central nervous system. In view of this fact, the following case is reported.

REPORT OF CASE

Clinical History.—A Chinese soldier, aged 39, presented himself at the Peiping Union Medical College Hospital, on Sept. 22, 1928, complaining of a genital sore of more than two months' duration. Examination at that time revealed a solitary, deep, nontender and indurated lesion about 1.5 cm. in diameter in the coronary sulcus. In the intergluteal fold there were multiple moist papules. Physical examination, particularly that of the nervous system, otherwise gave negative results. Dark-field examination of the discharge from the penile and intergluteal lesions showed the presence of *Spirochaeta pallida*. The Wassermann and Kahn reactions of the blood were both strongly positive. The spinal fluid was clear and colorless with a pressure of 112 mm. of water, and a cell count of 12 lymphocytes per cubic millimeter. The Wassermann reaction, Ross-Jones test, and colloidal gold and gum mastic curves were all negative. The patient was given 0.3 Gm. of arsphenamine intravenously.

The lesions on the penis and in the intergluteal region disappeared completely within ten days after the injection of arsphenamine. The patient did not return for further treatment until about two and one-half months later (Dec. 6, 1928), when he was admitted to the hospital with the chief complaint of headache.

On Nov. 20, 1928, the patient gradually began to suffer from headache without previous ill health or warning. The headache was diffuse and constant, tending to be localized with greater intensity over the vertex and the left half of the scalp, particularly behind the left ear. At times, the headache took the character of severe, throbbing, neuralgic pain, in association with which there were attacks

*Submitted for publication, July 15, 1929.

* From the Division of Dermatology and Syphilology of the Department of Medicine, Peiping Union Medical College.

1. Oppenheim, H.: Text-Book of Nervous Diseases, ed. 5 (translated by A. Bruce), London, T. N. Foulis **1**:308, 1911.

of excessive perspiration over the right side of the face, neck and upper part of the trunk.

On Nov. 23, the neck became stiff and tilted toward the right side. At the same time, the patient noticed pain in the left suboccipital region, on the left side of the back of the neck and in both shoulders. The pain was worse in the left shoulder and occasionally radiated down the entire left upper limb.

On Nov. 26, the left extremities were found to be weak, and there was a tingling sensation over the right leg. At no time had the patient felt feverish, and there had been no disturbance of urination or defecation.

The family, marital, past and personal histories were not important.

Physical Examination.—When examined on Dec. 6, 1928, the sixteenth day of the present illness, the following physical observations were made:

The patient was well developed and muscular. He did not look ill, but his expression was that of one suffering from severe headache. The left lung revealed some impairment of percussion note at its apex posteriorly. The liver was enlarged 7 cm. below the costal margin in the right midclavicular line and was firm, smooth and nontender. The temperature was 37.4 C.; the respiration rate was 20, and the pulse rate 100.

Neurologic Examination.—The patient was dull. There was no disorder of speech. The memory for remote and recent events was good, and he responded to questions readily.

The head was semiflexed toward the right side, the muscles of the right side of the neck being in a state of tonic contraction. Bending the head toward the left caused pain in the right side. There was no definite paralysis of any of the muscles involved.

Except for contraction of the left pupil and partial closure of the left palpebral fissure, the function of the cranial nerves was normal. The left pupil, however, was round and reacted to light and distance.

The motor power of the left extremities was considerably reduced in all movements, but there was no complete paralysis. When walking, the patient dragged the left leg with slight spasticity. There was no involuntary muscular contraction.

Both anteriorly and posteriorly there was complete loss of sensation to pinprick and temperature, extending from the level of the first intercostal space caudally and affecting the right extremities and the right half of the trunk to the middle line. Above the upper limit of the analgesia and thermanesthesia was a zone of hypalgesia about 3 cm. wide. Light touch and pressure were well appreciated. No area of hyperesthesia was demonstrable (fig. 1). The left suboccipital region and the left side of the back of the neck were tender to touch but not inflamed, though the soft tissues seemed to be somewhat bulged. There was spontaneous shooting pain over the vertex and the left half of the scalp—particularly around the left ear, in both shoulders and in the entire left upper limb. Position of the extremities on active and passive movements was quickly and easily recognized. The vibratory sense was intact.

The abdominal and cremasteric reflexes were absent on the left side, while the tendon reflexes on this side were all hyperactive. Ankle clonus, Babinski and Kernig signs were not obtained in either leg.

The finger-to-finger and heel-to-knee tests gave negative results. There was no Romberg sign or ataxia.

The right half of the head and the neck was somewhat flushed and profusely sweating. Otherwise the moisture and temperature of the cutaneous surface were normal. There was no evidence of trophic disturbance.

The urinary and anal sphincters were under good control.

Laboratory Examinations.—Urine: Routine urinary examinations always gave negative results.

A phenolsulphonphthalein test revealed normal function.

White cell counts, red cell counts, hemoglobin determinations and differential counts were always normal.

Ova of *Ascaris* were present.

The Wassermann and Kahn tests of the blood both gave strongly positive results.

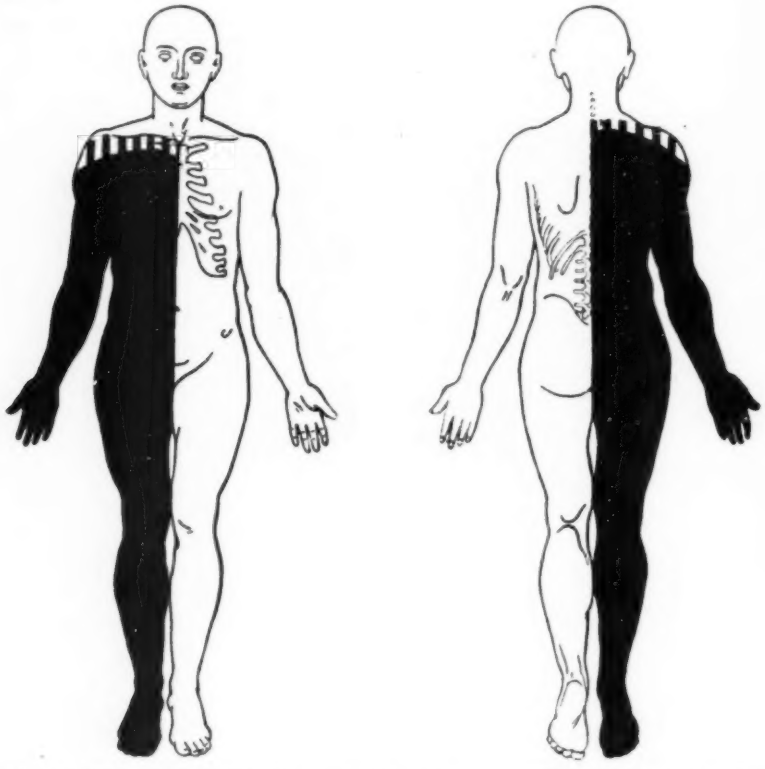


Fig. 1.—The sensory disturbances before treatment. The striped area indicates partial loss of sensation to pain and black area total loss of sensation to pain, heat and cold.

The fluid was cloudy, and the pressure was 125 mm. of water. The cell count was 1,080 per cubic millimeter, the cells being chiefly lymphocytes. The Ross-Jones test gave a positive result. The Wassermann reaction, with the Kolmer technic was 44444 in 0.5, 0.25, 0.125, 0.0625 and 0.03125 cc. of spinal fluid, respectively. The colloidal gold curve was 4455210000. Cultures of the spinal fluid showed no growth.

A phenoltetrachlorphthalein test showed a retention of 2 per cent of the dye at the end of one hour.

In the roentgenogram, there was no evidence of bone lesion or other pathologic condition in the cervical region and upper part of the lung.

Clinical Course and Treatment.—On December 8, the left cremasteric reflex could be elicited, but it was still much less active than that on the right side. A second lumbar puncture revealed somewhat cloudy spinal fluid with a pressure of 175 mm. of water. Compression on the right jugular vein raised the pressure to 350 mm., that on the left raising it to 200 mm. The patient was given 0.6 Gm. of neoarsphenamine intravenously.

On December 10, the mental condition began to clear, and the neuralgic pain over the vertex was no longer complained of. The muscular power of the left limbs was slightly improved. A second injection of neoarsphenamine, 0.6 Gm., was given.

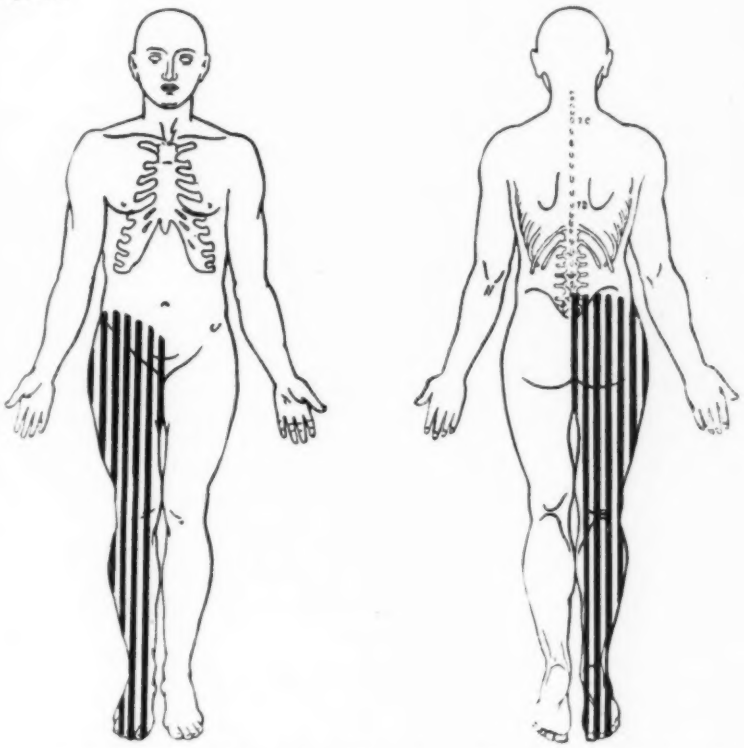


Fig. 2.—The sensory disturbances fifteen days after treatment was begun. The striped area indicates partial loss of sensation to pain.

On December 12, the tenderness at the left suboccipital region was much less intense and could be provoked only on deep pressure. The spinal fluid was slightly turbid, with a pressure of 175 mm. of water, which rose to 275 mm. when the right jugular vein was pressed and to 225 mm. when the left one was pressed. The cell count was 540 per cubic millimeter. The Wassermann reaction was 44420.

On December 14, the throbbing pain around the left ear disappeared. There was no more sweating over the right side of the face. The left pupil was still slightly smaller than the right. The neck was free from pain and could be moved freely in all directions. The muscular power of the left extremities was

markedly improved. The sensation to temperature and pain returned on the right side over the cervical and the first four thoracic segments, anteriorly and posteriorly. A third dose of neoarsphenamine, 0.6 Gm., was administered.

On December 18, the patient received a fourth injection of neoarsphenamine (0.6 Gm.) and showed more recovery from the disturbances of cutaneous sensibility.

On December 23, the muscular power of the left limbs was equal to that of the right. The tendon reflexes were normal and equal on the two sides. On the entire right side of the body perception of cold and heat began to return, but there was still hypalgesia from the first lumbar segment downward (fig. 2). The patient was then given an injection of 0.4 Gm. of arsphenamine.

On December 26, the spinal fluid was clear. The pressure was 200 mm. of water when the right jugular vein was compressed and 170 mm. when the left one was compressed. The cell count was 50 per cubic millimeter. The Ross-Jones test gave a positive reaction. The Wassermann reaction was 44300. The colloidal gold curve was 5555520000 and the gum mastic curve, 2342100000.

On December 27, when the patient was discharged from the hospital, the pupils were equal and all forms of sensation had become normal.

COMMENT

The high pleocytosis, 1,080 lymphocytes per cubic millimeter, indicated an acute and severe meningitis. The absence of evidence of cranial nerve palsy and irritation of the vertex of the brain suggested that in all probability only the spinal meninges were much affected. The strongly positive Wassermann reaction of the spinal fluid and the response of the patient to antisyphilitic treatment warranted the conclusion that the spinal meningitis was syphilitic in origin.

The small amount of arsenotherapy the patient had received during the early secondary period of the syphilitic infection and the differences in the observations at the neurologic and spinal fluid examinations before and after the development of the Brown-Séquard syndrome inclined us to attribute the meningitis to the recurrence of active syphilitic infection consequent on inadequate therapy.

This type of precocious neurosyphilis has been given the name of neurorecurrence or neurorezidive.[2] The general conception of its pathogenesis, as originally held by Ehrlich[2] and recently amplified by Moore,[3] is that inadequate treatment with arsphenamine in cases of early syphilis is particularly apt to be ineffective in destroying the *Spirochaeta pallida* in the central nervous system because of the high impermeability of nerve tissue to this drug. The sudden partial destruction of spirochetes suppresses the normal body defence reactions and deprives the patient of the immunity he would otherwise develop. Under such circumstances, the organisms remaining unaffected in the nervous system are free to multiply and, after a period of time varying from one to six months, may produce clinically demonstrable lesions, especially of the basal cerebral meninges and contiguous cranial nerves.

The clinical manifestations of the patient were those of both leptomeningitis and pachymeningitis. The differences in the elevation of the intraspinal pressure induced by compression of the jugular veins indicated that there was leptomen-

2. Ehrlich, P.: Ueber Salvarsan, München. med. Wchnschr. **58**:2481, 1911.

3. Moore, J. E.: The Relation of Neurorecurrences to Late Syphilis. A Clinical Study of Eighty-One Cases, Arch. Neurol. & Psychiat. **21**:117 (Jan.) 1929.

ingitis with the formation of adhesions in the subarachnoidal space. The presence of pachymeningitis was evidenced by the radicular pain from a considerable number of nerve roots as manifested by the neuralgia of the scalp, neck, shoulders and entire left arm.

The stiffness of the neck might have been due to upper cervical neuritis. Elsberg [4] stated that in cases of high cervical tumors the pain from a diseased condition of any of the cervical roots may be severe enough to make the neck so rigid that often the question of actual involvement of the bony structures has to be considered.

The marked tenderness in the left suboccipital region and the left side of the back of the neck was, in our opinion, due to a localized acute periostitis of the underlying osseous structures, although the roentgenogram did not reveal such bone pathology. According to Elsberg,[5] however, this condition is frequently present in cases of cord tumor, and the cause is thought to be irritation of the root of the sensory nerve supplying the spinous processes of the vertebrae. Starr [6] observed that upper cervical neuritis may produce intense occipital neuralgia which is attended by extreme sensitiveness of the great occipital nerve to pressure. This cervico-occipital neuralgia is rare. Jelliffe and White [7] have cited that in Remak's review of 15,000 cases of peripheral neuralgia only fifty were in the cervico-occipital region.

From the localization of the motor and sensory disturbances, it must be inferred that the meninges were most severely involved in the left middle cervical region, at which place there was either a restricted extension of the inflammatory process into the substance of the spinal cord or sufficient external pressure to interfere with the functions of the left pyramidal and spinothalamic tracts in the lateral columns, but not with those of the fibers in the posterior columns, as evidenced by the preservation of the tactile, muscle and vibratory senses.

The involvement of the sympathetic system, as shown by the oculopupillary changes and the excessive sweating over the right side of the face and neck and the right half of the upper trunk, indicated that the meningitis extended as low down as the upper thoracic region. It is generally recognized that the cervical sympathetic ganglia are connected with the spinal cord, not through the cervical roots, but through the first and second thoracic roots.

SUMMARY

A Chinese man with chancre and moist papules received one injection of 0.3 Gm. of arsphenamine during the third month of a syphilitic infection. At this time there was no clinical or serologic evidence of neurosyphilis. Two and one-half months after the administration of the antisyphilitic treatment, the patient developed cervical nerve root pains, evidence of impairment of the function of the sympathetic system, and motor and sensory disturbances of the Brown-Séquard type, together with signs of intensely acute syphilitic meningitis in the spinal fluid. The patient recovered in three weeks after being treated with 2.4 Gm. of neoarsphenamine and 0.4 Gm. of arsphenamine.

---

4. Elsberg, C. A.: Tumors of the Spinal Cord, New York, Paul B. Hoeber, Inc., 1925, p. 261.

5. Elsberg (footnote 4, p. 295).

6. Starr, M. A.: Organic and Functional Nervous Diseases, ed. 3, Philadelphia, Lea & Febiger, 1909, p. 171.

7. Jelliffe, S. E., and White, W. A.: Diseases of the Nervous System, ed. 4, Philadelphia, Lea & Febiger, 1923, p. 430.

As to the anatomic pathology, we believe that there was a diffuse leptomeningitis and pachymeningitis in the cervical and upper thoracic regions of the spinal cord, with the formation of adhesions in the subarachnoidal space and pressure on the upper cervical nerve roots. The interference with the left pyramidal and the left spinothalamic tracts seems to have resulted from the invasion or compression of the lateral columns of the spinal cord by the intense meningeal inflammation at the middle cervical region.

We are inclined to attribute the acute recurrence of the syphilitic infection to the insufficient arsenotherapy the patient had received during the early secondary course of his syphilitic infection and to classify the case as one of syphilitic neurorecurrence.

QUANTITATIVE ESTIMATION OF TOTAL PROTEIN OF CEREBROSPINAL FLUID

A Modification and Improvement of a Previously Described Method *

G. ALEXANDER YOUNG, M.D.; A. E. BENNETT, M.D.; J. M. CHRISTLIEB, M.D. and JOHN T. MYERS, M.D., PH.D., OMAHA

In a previous report,[1] we described a new practical method of quantitative total protein estimation in cerebrospinal fluid. We wish to correct some errors in this method that have been learned by further investigation and also to describe a modification of the method. This modification has proved to be a more accurate and simpler technic than that previously described.

The original method was by precipitation of protein in cerebrospinal fluid by 95 per cent alcohol, acetic acid and heat. The resultant precipitate was centrifugated in a capillary-tipped vaccine tube and the total amount of protein measured in hundredths of a cubic centimeter. This method has proved of practical clinical value and a definite improvement over the qualitative tests for globulin.

In working with other protein precipitants we have found that the original method was not a total protein method, but probably a total globulin precipitation, because when other reagents such as phosphotungstic acid were added to the supernatant fluid we found that more protein was precipitated.

Phosphotungstic acid has been proved to be a total precipitant for proteins. Boggs,[2] in using this acid as a precipitant for proteins in milk, found that the supernatant fluid gave no test for protein by the Kjeldahl method. In over 300 determinations he found a mean difference from the Kjeldahl method of only 0.2 per cent. Tsuchiya,[3] in working with protein precipitation in milk, devised the following formula: phosphotungstic acid, 1.5 Gm.; hydrochloric acid (concentrated), 5 cc.; ethyl alcohol, sufficient to make 100 cc. This reagent has been

* Submitted for publication, June 17, 1929.

* From the Neurology and Pathology Departments of the University of Nebraska Medical College.

1. Young, G. Alexander, and Bennett, A. E.: Studies on the Quantitative Estimation of the Total Protein Content in Cerebrospinal Fluid, Am. J. M. Sc. **172**:249 (Aug.) 1926.

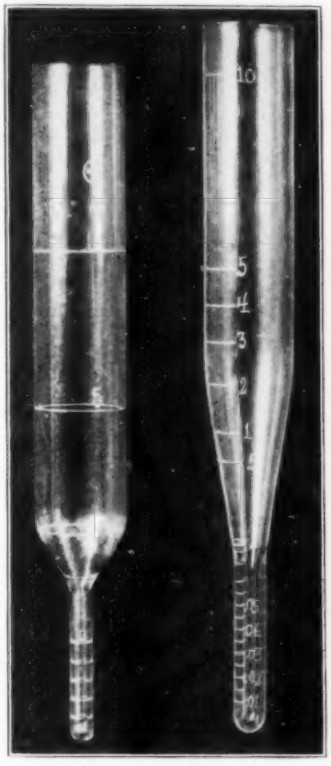
2. Boggs, T. R.: A Simple Method for Quantitative Determination of Proteid in Milk, Johns Hopkins Med. Bull. **17**:342, 1906.

3. Tsuchiya, I.: A New Volumetric Protein Determination in Milk, Zentrabl. f. inn. Med. **29**:105, 1908.

known as Tsuchiya's reagent. Mattice[4] confirmed the results of total precipitation of protein with Tsuchiya's reagent in urine and found it much more accurate than Esbach's reagent for quantitative albumin tests.

We have found that Tsuchiya's reagent precipitates from 25 to 33.3 per cent more protein from cerebrospinal fluid than the alcohol and acetic acid method. Furthermore, we have determined that the supernatant fluid shows no positive test for protein by the biuret method.

Our technic for the use of Tsuchiya's reagent in total protein estimation of cerebrospinal fluid is as follows: To 1 cc. of cerebrospinal fluid in a capillary-tipped Hopkins vaccine tube is added 2 cc. of Tsuchiya's reagent. After standing



On the left is shown the Hopkins vaccine tube; on the right, the modification with more sloping sides and more accurate calibrations of the tip.

for about ten minutes, the contents of the tube is then centrifugated for five minutes at about 2,000 revolutions per minute and a reading taken. Dr. F. W. Constable, of Providence, R. I., has suggested to us a modification of the ordinary Hopkins vaccine tube and we are now using this type of tube, shown in the accompanying figure. This tube has more sloping sides and overcomes collection of precipitate at the junction of the large and constricted portions of the Hopkins tube, and has a larger tip; we have had them calibrated in 0.005 cc. instead of 0.01 cc., thus giving more divisions on the tip and more accurate readings.

4. Mattice, A. F.: The Quantitative Estimation of Albumin in the Urine, Arch. Int. Med. **5**:313 (April) 1910.

To determine what the readings on the tube corresponded to in terms of milligrams of protein per hundred cubic centimeters of cerebrospinal fluid, two of us (J. M. C. and J. T. M.) have carried out a series of protein determinations by various methods and compared the results arrived at by chemical determination with alcoholic acetic precipitation and with Tsuchiya's reagent. The accompanying table gives the results of these determinations.

These results were determined by taking the difference between the nonprotein nitrogen readings and total nitrogen readings by the micro-Kjeldahl method, which gave the actual protein nitrogen present in cerebrospinal fluid. By comparing the percentage of protein nitrogen estimated by volumetric reading with Tsuchiya's reagent and the Kjeldahl method, the determinations parallel each other closely.

Knowing that there is a total protein precipitate with Tsuchiya's reagent, we have standardized the readings of the calibrated centrifuge tubes. As the table shows, each 0.01 cc. volume of precipitate was equivalent, on the average, to 10.3 mg. of protein nitrogen per hundred cubic centimeters of spinal fluid.

Comparative Chemical and Precipitation Determinations of Protein Content

	Alcohol Acetic Readings in Terms of 1 Cc. of Spinal Fluid	Tsuchiya Readings in Terms of 1 Cc. of Spinal Fluid	Total Nitrogen in Milligrams per 100 Cc.	Nonprotein Nitrogen in Milligrams per 100 Cc.	Total Protein Nitrogen in Milligrams per 100 Cc.	Equivalent of 0.01 Cc. of Precipitate in Milligrams of Protein
1	0.03	0.037	57.00	14.30	42.70	11.3
2	0.015	0.015	33.25	15.00	18.25	14.5
3	0.0035	0.008	18.10	12.50	5.60	7.5
4	0.0025	0.005	16.65	14.28	2.27	4.5
5	0.005	0.008	22.70	15.00	7.70	9.7
6	0.0075	0.010	23.25	15.75	7.50	7.5
7	0.005	0.008	35.70	19.95	15.80	21.0
8	0.0025	0.005	23.00	12.50	7.50	15.0
9	0.0075	0.010	25.00	19.95	5.65	5.7
10	0.035	0.05	76.80	22.70	54.10	10.8
11	0.06	0.112	200.00	34.00	166.00	14.8
12	0.05	0.082	88.00	28.20	60.60	7.4
13	0.05	0.078	100.00	23.60	76.40	9.8
14	0.04	0.072	90.80	35.60	55.20	7.4
15	0.05	0.074	93.80	25.00	65.80	8.9
						10.3 average

The discrepancies seem very large, but this would be expected when comparing the accurate micro-Kjeldahl method with one which depends on the measurement of volumes of a precipitate. There are many factors which might change such a volume, among them the following: variations in the rate of the centrifuge, although the time seemed sufficient for complete packing; variations in the types of protein in the spinal fluid, some producing a flocculent, others a more granular precipitate, the latter making a smaller volume for the same quantity of protein; variations in the rate of precipitation due to speed of mixing and temperature which might make changes in the compactness of the packed precipitate; variations in calibration of the Hopkins vaccine tubes. As stated before, we are now procuring more accurate tubes similar to that illustrated.

However, the technic seems satisfactory for clinical purposes, as it is very simple, quick and sufficiently accurate for all practical purposes.

The present modification is an advance over the technic previously described, because it gives more complete protein precipitation; it requires no heating and does not have to be transferred from one tube to another.

We have found normal readings to vary from less than 0.01 cc. or 10 mg. or less per hundred cubic centimeters, to 0.02 cc. or 20 mg. per hundred cubic centimeters. In our previous report [1] we were in error in the calculation of the milligrams of protein per hundred cubic centimeters. In converting the readings on the tube to milligrams per hundred cubic centimeters we reported all readings

in milligrams per hundred cubic centimeters consistently five times too high. We stated that the fluids normally contained from 25 to 75 mg. per hundred cubic centimeters when the protein content with the alcoholic acetic method should have been from 5 to 15 mg. With the present use of Tsuchiya's reagent the normal range is from 5 to 20 mg. per hundred cubic centimeters. These figures are more in keeping with Ayers'[4] revised figures in the quantitative estimation of total protein. For clinical purposes we have not been in the habit of recording the readings in milligrams per hundred cubic centimeters but in hundredths of a cubic centimeter and have considered the upper limit of normal with the present method as 0.020 cc. or, as calculated by the standardization of the table, 0.020 × 10.3 or 20.6 mg. per hundred cubic centimeters.

SUMMARY

We have reported a rapid, simple, practical method of total protein estimation of cerebrospinal fluid. This method is a modification and improvement of a previously described technic. Our present technic has proved more accurate and is definitely a total protein determination. The principle is the precipitation of protein by Tsuchiya's reagent, and measuring the precipitate volumetrically in calibrated capillary-tipped vaccine tubes.

News and Comment

POST-GRADUATE STUDY IN NEUROLOGY AND PSYCHIATRY IN VIENNA

A six weeks' course in neurology and psychiatry and associated branches will be given between June 23 and July 31, 1930, inclusive. Applications should be sent to Docent Dr. E. Spiegel, Falkestrasse 3, Vienna I, Austria.

Obituaries

C. FLOYD HAVILAND
1875–1930

The sudden death of Dr. C. Floyd Haviland on Jan. 1, 1930, in Cairo, Egypt, deprived American psychiatry of a worker of national reputation whose real worth was appreciated only by those who knew him best. He has left behind achievements, and not the least of these was his influence on his friends and on those who worked with him.

Floyd Haviland was born in Spencertown, N. Y., on Aug. 15, 1875. His father is a physician, still in practice. With this background a medical career was the natural one and for this he trained himself, graduating from the Medical School of Syracuse University in 1896. His earliest interest was psychiatry, and in 1897 he was appointed medical intern at Manhattan State Hospital on Ward's Island. American psychiatry has made much progress in the thirty years during which Dr. Haviland was associated with it; in this progress he participated very actively and he led not a little of it. The story of Dr. Haviland's medical life could be used as a ground-work for writing a history of psychiatric advance in America in the past thirty years. He was a part of nearly all of it.

Dr. Haviland served well a long psychiatric apprenticeship at Ward's Island from 1897 to 1910, when he left the post of second assistant physician at Manhattan State Hospital to become first assistant physician at King's Park State Hospital. Here he continued to serve with that sincerity and simplicity which were to be the traits that marked his life, and are the things of his that will be remembered longest by his friends.

It was while Dr. Haviland was at King's Park that this country saw a radical departure in the care of the insane which has reaped a happy harvest. The National Committee for Mental Hygiene started its campaign to improve the hospital care of the insane. The first step consisted of surveys of conditions attending the care of the insane in county asylums and state hospitals of the separate states. The task was difficult. Conditions in many places were deplorable and hedged around with politics and special privilege. The work called for men of long training, fearless honesty, diplomacy and a great capacity for making friends. Dr. Haviland was chosen, in 1914, to make a survey in Pennsylvania. The work was well done, and that survey was one of the most important factors in the establishing of the National Committee as a real force in American medical science.

C. FLOYD HAVILAND, M.D.

1875—1930

In 1915, Connecticut recognized Dr. Haviland's ability by appointing him superintendent of the state hospital at Middletown, which position he held for six years. The prestige of the hospital grew under his hand and it became more a part of the life of the city.

In 1921, the New York State Hospital Service recalled Dr. Haviland to take over the duties of chairman of the State Hospital Commission. This honor came to him unsought, as had the others. Again the work was difficult, requiring those characteristics that were an innate part of Floyd Haviland. He had the fearlessness, the sincerity, the honesty and, what was of equal importance, the ability to make friends; friends for himself and, what to his mind was more important, friends for the insane poor of the state, in whose interests his entire life was to be spent. Radical changes were taking place at Albany and in the State Hospital Service, and Dr. Haviland guided them wisely. Under his guidance appeared the modernization of the State Hospital Commission into the State Department of Mental Hygiene, and the State Psychiatric Institute realized the ambitions the state held for it in the new building that towers on Washington Heights. Dr. Haviland lived to see both of these dreams of his realized.

In 1926, Dr. Haviland resigned from the State Hospital Commission to become superintendent of the Manhattan State Hospital on Ward's Island. He was tired, and his health was not the best. He longed to get back to what had always been his prime interest—the care of the insane. He hungered for contact with patients. Ward's Island, his first hospital, had always been home to him. He came home. He was happy there. He set about to build up his staff. He fought valiantly the inroads of the great city on his hospital, for he believed the insane poor of New York should keep their hospital within the city. It may have been a losing battle, but bravely it was fought. He died while on a vacation.

Time does not permit mention of all of Dr. Haviland's connection with medical societies. He was a former president of the American Psychiatric Association, director of the Executive Committee of the National Committee for Mental Hygiene, chairman of the New York State Mental Hygiene Committee, a member of the American Psychopathological Association, the American Genetic Association, the American Neurological Association, the New York Neurological Society and the New York Psychiatric Society, and at his death he was president of the New York Society for Clinical Psychiatry. He had been clinical professor of psychiatry at Columbia University since 1927.

Floyd Haviland's death leaves a gap in New York psychiatry that will be hard to fill. Those who relied on him feel his passing deeply. We looked forward with hope to his guidance and counsel in the future. What we feel most deeply is the loss of a friend.

HERMAN HENRY HOPPE, M.D.

1867-1929

Dr. Herman Henry Hoppe died suddenly on Oct. 20, 1929, as a result of coronary occlusion, omnious symptoms of which had been noted for several weeks previously.

Dr. Hoppe was born in Cincinnati on Jan. 4, 1867, the son of Dominic and Mary (Dusterburg) Hoppe. At the age of 13, he entered St. Xavier College, from which he was graduated in 1886. He then became a student of medicine at the Ohio Medical College, graduating second in a class of ninety in 1889. After an internship of eighteen months in the Cincinnati General Hospital, he went abroad, spending the first summer studying pathology under Professor Recklinghausen at Strassburg. In the fall of the same year he went to Berlin where, combined with other studies, he acted as voluntary assistant to Professor Oppenheim, continuing his work with this great teacher until he left Europe in August, 1892. It was under the inspiration and guidance of Professor Oppenheim that Dr. Hoppe laid a sure and broad foundation in the discipline of clinical neurology and neuropathology, which was the determining factor of his career as a neurologist.

Dr. Hoppe began the practice of neurology in 1892. He was appointed on the staff of the Cincinnati General Hospital in 1894. His first teaching position was that of lecturer on nervous diseases in 1894, and in 1900, when the old Ohio and the Miami Medical Colleges merged and became the School of Medicine of the University of Cincinnati, he was made professor of nervous diseases and head of the neurological department at the Cincinnati General Hospital, in which capacity he continued until his death. He was a member of the Academy of Medicine of Cincinnati, the Ohio State Medical Association and the Mississippi Valley Medical Association, and was for many years an active and contributing member of the American Neurological Association, rarely missing any of its meetings. Notwithstanding the demands of a large practice, Dr. Hoppe found time to make many contributions to the literature of his chosen field.

In 1895, Dr. Hoppe married Hermanie Richard, daughter of a physician. She died, leaving two daughters, Rosemary Hermanie and Elizabeth Jacqueline.

From the personal standpoint there remains little to add, except to pay tribute to a colleague who, during an unusually busy professional career, labored with unflagging energy, boundless optimism and strict devotion to the highest demands of his profession, advancing in every possible manner the importance of neuropsychiatry in his community.

(Photograph by J. Anthony Bill, Cincinnati)

HERMAN HENRY HOPPE, M.D.

1867–1929

Abstracts from Current Literature

PHYSIOLOGIC INVESTIGATIONS AFTER RESECTION OF THE RIGHT CEREBELLAR HEMISPHERE IN MAN. M. H. FISCHER and O. PÖTZL, Ztschr. f. d. ges. Neurol. u. Psychiat. **119**:163 (March) 1929.

Jaksch and Schloffer reported a case of resection of a large part of the right cerebellar hemisphere because of an infiltrating tumor. After three years, the patient is alive and in good condition, so that Fischer and Pötzl thought that they had a good subject for research into the changed relations to be noted after removal of the right cerebellar hemisphere, and into the compensatory mechanisms to be found in other parts of the nervous system. They were interested largely in the equilibratory reactions.

The patient, aged 43, complained of pains in the occiput, and vertigo on rotation or quick movement. Early in the disease he had periods of vertigo lasting from four to five minutes. His gait became more and more difficult, and in the attacks of vertigo he felt as if he was being pulled to the right, though he fell constantly to the left. After about six months, he was unable to walk. Examination at this time showed choking of 3 and 2 diopters. He had generally increased reflexes, bilateral ankle clonus and a Babinski sign present at times on the left and at times on both sides. He was able to walk only with support, and fell to the left constantly. Muscle tone was decreased in all the extremities, but more so on the left. The head was held in a fixed attitude, bent to the left and slightly rotated to the right. In seated and prone postures there was a definite forced attitude of the body to the left. The cochlear portions of the eighth nerve were normal. Vestibular investigation showed a slight spontaneous vertical nystagmus upward and downward, spontaneous deviation of both arms to the right, forced attitude of the head to the left and back, slight ataxia in the finger-to-nose test and bradyteleokinesis on both sides, more marked on the right. An operation was performed and a cerebellar cyst found in the right cerebellar hemisphere. It was not removed. After the operation the deviation of the head and body to the left was less marked, there was no longer any pull to fall to the right and there was a slight tendency to pass point with the right hand to the left; there was no vertigo or hypotonia as before the operation, and nystagmus was present only on deviation. After convalescence, the patient was again operated on, and this time cerebellar tissue was removed. The outer two thirds of the right cerebellar hemisphere was cut away, the incision running 1 cm. lateral and parallel to the incisura marsupialis, taking a part of the tonsil and extending on to the flocculus. After the cerebellum was removed there remained on the right side: (1) a small zone along the incisura marsupialis, (2) a small piece of tonsil, (3) a piece 2 cm. wide toward the cerebellopontile angle and (4) a piece 2 cm. wide toward the superior vermis. The nucleus dentatus was left intact. Following the operation the nystagmus remained as before. A slight facial weakness was present but disappeared after two days. Muscle tone was decreased as before the operation. There was bilateral ankle clonus, and often a Babinski sign. There was definite adiadokokinesis, especially of the right hand, and a tendency of the left arm to pass point. The forced attitude of the head to the left disappeared. Vestibular investigation after operation showed spontaneous nystagmus upward and downward. Bárány stimulation when weak produced no responses, but stronger stimuli produced normal reactions, though weaker than in the normal person. Shortly before discharge, gait was normal.

From the observations in this case Wodak came to the conclusion "that the cerebellum, at least the neocerebellum, is not absolutely necessary for the production of the so-called vestibular tonic reflexes." This conclusion was reached because there was no time in this case at which the vestibular tonic reflexes were actually lacking. In this respect the case agrees with that of de Stella in which, after a

cerebellar resection, the eighth nerve reflexes, lost before operation, were again produced. In de Stella's case the entire right cerebellar hemisphere with an angle tumor, including the nucleus dentatus, was removed. After operation the vertigo, vomiting and spontaneous nystagmus disappeared, but there followed adiadokokinesis, ataxia, asthenia and atonia on the side of the lesion. The vestibular reactions reappeared though they were weaker than normal. De Stella concluded: (1) The cerebellum is not the central organ of the nervus vestibularis. (2) The labyrinthine reflexes do not pass by way of the cerebellum. There is rather an accessory tract which passes through the latter. (3) By way of this tract the cerebellum exerts a regulating effect on the labyrinth, movements and coordination. He says nothing of the tonic labyrinthine reflexes, and the case reported by Fischer and Pötzl is therefore the first to show that these remain intact when the cerebellum is removed.

A point of interest is the fact that in the case reported the patient fell to the left, away from the lesion. It is well known that in unilateral cerebellar disease spontaneous falling is by far most frequently toward the sound side. There are always a small number of cases in which the direction of the fall is not to the side of the cerebellar lesion, and a number in which it varies during the period of observation. Rhese has found that "cerebellar foci, before they destroy the falling tract, can produce irritative effects on this tract from a distance." If such an effect is produced only on the vestibular nuclei of the same side, the fall must be toward the diseased side; irritation of the specific "falling tract" in the cerebellum causes a fall to the healthy side due to the crossed connection between this tract and Deiter's nucleus. Irritative effects may be produced on both sides, thus causing an uncertain effect. In the case of Fischer and Pötzl only once did the patient fall to the side of the tumor. Rhese believes that there are two groups of centers in the vermis: (1) a center for movements of the trunk lateral and backward, and (2) a center for the movements of the trunk lateral and forward. Pötzl explains the fall to the healthy side in the case reported as being due to an over-excitement of these centers, or to an inhibition of the excitatory stimuli of the left vestibular nuclear area. This inhibitory effect would appear to go by the cerebellar cortex and median cerebellar nuclei to the right and left vestibular nuclei in a specific way: the inhibitory effects on the tonic reflexes of the upper extremity corresponded to the side of the cerebellar focus, while the inhibition of postural reflexes of the head and trunk corresponded to the side opposite the focus. This would indicate that the right neocerebellar region of the upper extremity of man sends stimuli to the left vestibular nuclei, resulting in a hypertonia of the left arm musculature, while it sends stimuli to the right vestibular nuclei resulting in deviation of the arm to the right.

How can one explain the subjective sensation of falling to the right, the fall being actually to the left? Either the fall to the left was compensatory for the feeling of falling to the right, or the right vestibular nuclei were stimulated as the left were inhibited. The latter is the more likely.

Pathologic Anatomy of the Excised Tumor.—Histologic study of the tumor revealed an angioplastic tumor with cyst formation of the type described by Lindau. Serial sections were made. These revealed that the tumor occupied the right cerebellar lobe almost exactly in the middle of the lobus biventer. The nucleus dentatus was not seen in serial sections though it may have been injured by cicatricial tissue after the operation. Miliary hemorrhages were seen at the edge of the tumor, and some of these may have involved the dentate nucleus. At any rate, whatever the injury, it did not correspond in extent to that of de Stella's case. The Purkinje cells in the cerebellar tissue removed had been replaced practically by a pseudogranular layer. The projection fibers were injured. A partial transection of the pontile fibers of the cerebellum was accomplished by the operative removal. Hence there was also injury to the olivocerebellar fibers, and to the projection fibers between the right lobus biventer and corresponding parts of the right dentate nucleus. It is questionable whether the spinocerebellar system was injured, but it is certain that the median vestibulocerebellar system was not harmed.

After the operation and before complete recovery the patient made a few complaints. He experienced a tickling sensation in the stomach, deep in this region. This sensation came when he turned the entire body to the right. If he held his head and turned the body to the right it did not appear, and if he turned the head without the body the same was true. He had a subjective sensation as if he had to move the head and body as a unit. He complained also of dysarthric speech, but this was not evident save, at times, for stuttering. This calls to mind Stenver's views of the relation between cerebellar speech disturbance and right cerebellar foci. The gait was unsteady. Both legs were hypermetric on walking, the left more than the right. The left leg swung into the midline and almost crossed the right. The right attempted to compensate.

The most striking feature was the stiff attitude of the head which was rotated a little to the left, and flexed toward the left shoulder and slightly backward. In other words the head was held over to the healthy side. Fischer and Pötzl suggest a predominance of certain neck muscles in the maintenance of this position. Another feature was the deviation of the left arm with the arms extended, while the right arm did not deviate at all. The left arm fell lower than the right. When the head was rotated to the right both arms deviated to that side. This was less true to the left. Bending the head forward pulled the arms up a bit. Motor power was everywhere normal, without ataxia, tremor or adiadokokinesis. The patient was unable to move his head rapidly without turning his whole body also. Moving pictures showed that the head moved slowly and was always bent backward. Hearing was normal. On rotation there was a slight difference in the frequency of the after-nystagmus in the two directions, but not in its duration. The left arm deviated a few centimeters to the outside after rotation, but the right not at all. Caloric testing provoked horizontal rotary nystagmus to the left. Bending the head back 90 degrees produced a more severe vertical nystagmus. Bending the head 45 degrees toward the shoulder caused lateropulsion. No propulsion reflex was present. On looking down there was diagonal nystagmus to the right after douching both ears. Moreover, the deviation of the left arm disappeared and the right arm now deviated from 5 to 15 cm. outward. The eyes were normal. The optokinetic nystagmus in this case was so marked that the head and body turned so far about the long axis as to fall to the same side. When the patient was first tested by caloric tests he developed a tremor of both legs, which he was unable to stop and left him so weak that he could not stand. This was not reproduced after the first attempt. Speech was normal. Vibratory sense was better in the right extremity.

The significance of certain observations is: (1) The attitude of the head is important. It was held bent slightly back and flexed to the left. After median section in animals, extirpation of the vermis occurs and after total extirpation of the cerebellum, a marked opisthotonos. In animals, as in man, this is a symptom which endures. The direction of the pull, namely, backward, is the same as in involvement of the vermis. Though the latter was not directly injured in this case there was an indirect effect on the oral part of the vermis causing a pull of the head backward. It is noteworthy that the head was pulled to the left. In animals after extirpation of the cerebellum the head is bent to the left side of the extirpation and is somewhat rotated, with the fore paws deviating to the opposite side. The opposite was true in the case reported. The majority of cases in man have shown a deviation of the head to the side of the cerebellar lesion. Fischer and Pötzl attribute the difference to a tonus center in the cerebellum which causes an asymmetrical increase in the tonus of the neck musculature. (2) The deviation of the arm has been noted. This is attributed to the destruction of the lobus biventer, since this causes a deviation of the arm to the opposite side. The deviation is in part also due to a pathologic predominance of tonic stimuli sent out from the intact lobus biventer. The deviation described is not the same as vestibular deviation. (3) The pronation phenomenon of Hoff and Schilder was present. Fischer and Pötzl look on this as an Ausfall phenomenon due to the absence of the right cerebellum. It disappeared with radiation of the left hemi-

sphere by an Alpine lamp. Hoff and Schilder believe that the pronation sign is an example of the fact that the cerebellum supports tonus in unusual positions of the limbs. (4) The firm relation which existed between the movements of the head and trunk is also considered an Ausfall sign due to resection of the right cerebellar hemisphere. Bolk has shown a striking relationship between the size of the lobus simplex and the innervation and shape of the neck, e. g., in the giraffe. Within physiologic limits the head and trunk move as separate units in health, and the condition found in the case reported is a regression to the stage where the head and trunk moved as one. There is, of course, the possibility that the movement may have been due to injury of the neck muscles during operation with resultant cicatrix formation. The stronger interrelation of the head and body on turning to the left is probably due to the tonic influence of the cerebellum on the neck muscles by means of crossed innervation. (5) Despite removal of the cerebellar hemispheres, nystagmus, falling and the other vestibular reactions were elicited. These reflexes, therefore, do not pass by way of the cerebellum. Caloric tests showed that the right labyrinth was more excitable than the left, while the latter seemed more so as indicated by the deviation of the arms. The nucleus angularis and the nucleus of Rolier are implicated in nystagmus, so one must assume that a pseudovestibular reaction is produced, with the left Deiter's nucleus more excitable than the right. Fischer and Pötzl do not believe that the deviation of the arms in this case is a vestibular reaction. The intact left cerebellar hemisphere is in connection with the opposite red nucleus which receives impulses from it, something which the left does not receive. As a result of this asymmetry of excitation there follows a deviation of both arms to the side of the intact cerebellar hemisphere. Experimental evidence supports this view. Rothman found in cats and dogs that stimulation of the cortex caused no movement if the ipsolateral cerebellar peduncle was cut before its decussation in the midbrain. Sherrington has shown that in decerebrate cats stimuli produce effects only if the decerebration is oral to the red nucleus. If it is caudal to this, stimuli have no effect in the production of movements. (6) Sensory disturbances are of interest in the case of Fischer and Pötzl. On the right side of the body there was an intensification and prolongation of vibration sense. This correponded to a decrease of cerebellar activity and to the excised part of the cerebellum. The observations, which were checked many times, do not disprove the fact that lesions of the cerebellum are not associated with sensory change. They are either Ausfall phenomena, or in part due to an increased irritability as in the case reported. There was no disturbance of touch with the vibratory disorder.

Fischer and Pötzl state that the observations in the case reported do not disagree with any of the prevailing theories of cerebellar function. Of Luciani's triad of atonia, asthenia and astasia, only astasia was present in this case. There was no asthenia, either local or general. Dusser de Barenne and Rademaker have shown that asthenia is not part of the cerebellar complex. Fischer and Pötzl are unable to say that atonia was not present at all, but they are certain that it was not present in the recovered stage, after operation and thereafter. There are cases of adynamia (Marburg) in cerebellar disease, but this sign was not present here. This is not the same as atonia, however. The astasia of Luciani is not an inability to stand, but an inability to stand quietly and surely. In this sense there was an astasia both before and after operation. Fischer and Pötzl believe that there is an analogy between the postural deviations in their case and the anisosthenia of André-Thomas. If one holds fast to the Luciani concept the astasia may be explained as a combination of anisosthenia and defective reciprocal innervation (Tilney-Pike). There was no inhibition of automatic postures, as seen in progressive cerebellar disease, in this case, but there was a mild spontaneous deviation of the arms to the left as a remnant of this inhibition. Goldstein assumes that the cerebellum practices a supporting effect on the tendency of the arms to adduct and flex. He sees in this tendency the expression of a fundamental function of the cerebellum. If this function is injured, postures in

extension and adduction are facilitated. The past-pointing is outward on the side of the lesion.

The speech disturbance in this case of cerebellar disease is of interest. Dusser de Barenne believes that in man the cerebellum takes on a specific motor function in speech movements. Stuttering is seen in cerebellar disease, and in cases of atrophy there is a scanning speech, with the word broken up into its constituent parts. Fischer and Pötzl explain the speech disorder in the case reported by Stenver's idea of a connection between the right hand center and the right cerebellum. It is striking that in this case of neocerebellar removal there should be speech disturbance when the cerebellar arm centers are removed. The symptom might be indirect, but probably not. Brunner reported a case of bilateral cerebellar disease with a marked speech disturbance which consisted of a slow speech with the omission of many letters and syllables. After resection of the cerebellum the speech trouble improved due to compensation by the cerebrum. Bradyteleokinesis has been shown by Léri to be an important function of the cerebellum in the regulation of antagonistic innervation; it causes a shortening of the amplitude of movement. Léri believed that this influence on the antagonists is a function of the cerebellum, the cerebrum exercising an inhibitory influence on this activity. Finally, the disturbance of vibration in this case would indicate that the cerebellum, in addition to being the chief proprioceptive ganglion (Sherrington), also receives exteroceptive impulses.

ALPERS, Philadelphia.

THE MORPHOLOGY AND FUNCTIONAL INTERPRETATION OF THE OLIGODENDROGLIA. P. DEL RIO HORTEGA, Mem. Soc. Españ. Hist. Natur. **14**:5 (Dec.) 1928.

This is an important monograph illustrated with seventy-nine figures, many of which are photomicrographs, based on an extensive study of material prepared with silver carbonate, and with a new method (modification of the method of Golgi). The latter is as follows: Small blocks of tissue (from 2 to 3 mm. thick) are preserved in the following mixture: potassium bichromate, 3 Gm.; chloral hydrate, from 2 to 5 Gm.; 10 per cent liquor formaldehydi, 50 cc., for two or three days. They are quickly washed in distilled water, and immersed in 1.5 per cent solution of silver nitrate for two or three days. Other steps are as for the method of Golgi. This procedure is not specific for oligodendroglia since it also stains protoplasmic and fibrous astroglia. Nerve cells are also stained, but they appear of lighter color than the neuroglia. The best results were obtained in the cat and the dog, young and adult. Rabbits and human material were also used. Most of the figures in the article are copied from preparations obtained with this method.

For the staining of the oligodendroglia with silver carbonate, the author fixes the tissues in 10 per cent liquor formaldehydi with 1 or 2 per cent chloral hydrate, or an equal amount of other hypnotics (barbital, diallyl barbituric acid, sulphonmethane, phenobarbital, etc.) for from two to twelve days. Frozen sections are washed in water with a few drops of ammonia, stained with "strong" solution of silver carbonate (ten or fifteen minutes), washed in 60 per cent alcohol (from one to two minutes) and reduced with 10 per cent liquor formaldehydi.

The literature on the subject is fully reviewed and discussed in the first sections of the paper. The morphologic characteristics of the oligodendroglia cells (oligodendrocytes) are then given in detail. Oligodendrocytes are elements of variable size, either round, polygonal or pear-shaped, with a round nucleus surrounded by a small amount of cytoplasm prolonged into long, scantily branched processes. The aspect of the latter varies a good deal; however, in most cells they resemble much twisted, narrow ribbons, and in some places they are constricted and appear as filiform prolongations. The number of processes, as revealed by the modification of the method of Golgi, is larger than was thought at first, and their branching is quite elaborate in some cases. They may show small swellings or knots which correspond to points of bifurcation. The pro-

longations do not end on the blood vessels but are applied against the surface of the nerve fibers, where they form reticulated sheaths. Since oligodendrocytes are abundant, especially in the white matter, and their prolongations are more numerous and more elaborately branched than was at first believed, the plexus thus originated is extremely complicated. However, Hortega denies the existence of a glial syncytium. He believes that the processes of the fibrous astroglia end on the vessels and on the pia, while a few of the processes of the protoplasmic astroglia end on the vessels, but most of them are applied on the cell bodies and dendrites of the neurons. The prolongations of the oligodendrocytes, on the other hand, furnish sheaths for the nerve fibers in the gray and the white matter. Microglia cells are free in nerve tissue, and their processes occupy the interstices of the glial and neuronal meshwork.

Four types of oligodendrocytes are distinguished. The first type, termed by Hortega "oligodendrocytes of Robertson," occurs in the cerebrum, cerebellum and spinal cord. They are usually located near the nerve cells and blood vessels, and also in the interstices between bundles of nerve fibers with thin myelin sheaths. These cells are small (from 15 to 20 microns), round or polygonal; the cell body is beset with abundant, extremely thin prolongations. The latter become wider as they come into contact with the nerve fibers and are scantily branched.

The cells of the second type, "oligodendrocytes of Cajal," are larger (from 20 to 40 microns) and are found chiefly in the white matter. Their prolongations are not numerous; they are rather thick, and are applied on the surface of the nerve fibers, their direction being predominantly longitudinal. The processes are usually arranged as spirals wound around the nerve fibers in close contact with the myelin sheaths, and they constitute rings or small funnel-shaped structures, or else they branch on the surface of the sheath under the form of networks.

Cells of the third type, "oligodendrocytes of Paladino," are large and occur chiefly wherever there are thick myelinated fibers (cerebral and cerebellar peduncles, medulla, pons and spinal cord). They are not so abundant as the elements of the two preceding types, and possess from one to four thick prolongations and a smaller number of thinner processes. The prolongations spread on the surface of the nerve fibers, where they form networks of uniform thickness or are strengthened with rings or funnel-shaped structures. They usually follow a spiral course and are compared by the author with the tendrils of a vine. When the prolongations are branched the aspect of the networks is more complicated. Furthermore, the branches of the oligodendrocytes of this type have true funnel-shaped formations or intramyelinic septums.

Elements of the fourth type are much elongated, monopolar or bipolar cells, rather similar to the cells of Schwann of the peripheral nerves. The cell body is spindle shaped and is prolonged on the surface of the nerve fibers, which thus appear covered with laminar, fenestrated or reticulated structures, strengthened with rings and funnels. They occur between the nerve bundles of the peduncles, pons, medulla and spinal cord, among medium-sized and thick nerve fibers.

The four types of oligodendroglia form a series in which transitional forms are numerous. From a study of the rings and funnel-shaped structures Hortega concludes that such structures in the central nervous system are identical with the corresponding formations long known in the peripheral nerves.

Abnormal changes in the oligodendroglia are described. Autolysis is a general phenomenon after death. In this condition the oligodendrocytes appear swollen, and their processes may also swell and become disconnected from the cell body (clasmatodendrosis). Degeneration and reaction (hypertrophy and hyperplasia) of the oligodendroglia go hand in hand with corresponding processes of the astroglia. Hyperplasia of the oligodendroglia has been observed by the author in certain cases of paresis; increase in the numbers of oligodendrocytes takes place through direct division, and the proliferated elements constitute accumulations around degenerated neurons and around the vessels. Oligodendrogliosis is accompanied in these cases by a corresponding hyperplasia of the astroglia and the microglia. Endolysis or transparent tumefaction (acute swelling of Penfield and Cone) occurs in human

oligodendroglia, but it is at present impossible to say whether it is due to pathologic conditions or is originated during agony and increased after death. A study of two cases of oligodendroglioma indicates that pronounced swelling may occur in this condition. Turbid tumefaction, a type of cloudy swelling, occurs in some cases of tuberculous encephalitis; cells undergoing this change tend to fuse with each other, and in this way masses of vacuolated cytoplasm containing several nuclei are originated. In trypanosomiasis of the horse (mal de caderas) the oligodendrocytes appear swollen and filled with granules of variable size; the presence of two nuclei within the same cell and of isogenic pairs is regarded as evidence of cell division in this case. The changes mentioned, although of degenerative nature, do not end in the death of the cells; in fact the nuclei remain nearly normal or appear only moderately pyknotic. In other cases, however, there exists a marked destructive tendency, already indicated by Grynfeltt and Pelissier in senile processes, and extended to Schilder's disease by Bailey and Schaltenbrand. According to the observations of Hortega in one case of Schilder's disease, the oligodendrocytes appear round, swollen and filled with a homogeneous substance that stains light pink with toluidin blue. In a case of hydrocephalus similar phenomena were seen in areas in the vicinity of the ependyma of the ventricles. In spite of these facts the author doubts the existence of mucous degeneration in these cases. A more important feature in Schilder's disease is the decrease in numbers of the oligodendrocytes coincident with the disappearance of the myelin. The author suggests that absence of the latter may not be the result of degenerative phenomena but that it might be due to agenesis of the oligodendrocytes.

Certain activities of the oligodendrocytes, such as their tendency to store fat, phagocytosis and retention of iron (sideropexia), are also discussed. The author denies a phagocytic function in the oligodendroglia. Cells of this type of neuroglia, contrary to the observations of Méduna, do not take an active part in the formation of granulo-adipose bodies, and the fat droplets found in the oligodendrocytes by Struwe and other authors probably have an endogenous origin. The retention of iron (Eisenspeicherung), demonstrated by Spatz and Metz, Struwe, Malamud and Wilson, is regarded by Hortega as passive impregnation of the cytoplasm of the oligodendrocytes when hemosiderin is in a sol state, while this substance is retained on the surface of the cells when it is a gel state. According to the author, most of the products of hematic disintegration (Blutzerfalleisen) are taken up by the microglia. The same applies to the case of the iron of paresis (Paralyseeisen).

The morphologic and genetic relationship of the astrocytes and the oligodendrocytes is reviewed in another section of the paper. The author thinks that astrocytes and oligodendrocytes are independent types that arise from the same stem cells but soon differ morphologically and functionally. His ideas on this important subject are summarized as follows:

- neuro-epithelium
  - neurocytoblasts → neuroblasts → neurons
  - gliocytoblasts
    - astroblasts
      - astrospongioblasts → astrospongiocytes (protoplasmic neuroglia)
      - astroinoblasts → astroinocytes (fibrous neuroglia)
    - oligodendroblasts → oligodendrocytes (oligodendroglia)

The oligodendrocytes seem to be the last differentiated elements of the neuroglia, since their formation can still be seen in newly born and very young animals. The oligodendroblasts seem to apply themselves to the surface of one or more nerve fibers and migrate passively during the growth of the latter. In this way series or rows of oligodendrocytes are formed, and these series cannot be interpreted as due to active migration of the oligodendroblasts. According to the author, there are no transitional stages between the astrocytes and the oligodendrocytes, but there is a cell type with ambiguous characteristics, found chiefly in the white matter of the brain. Cells of this type resemble oligodendrocytes on account of the size and shape of the cell body, but they have numerous prolongations,

repeatedly branched and with characteristics similar to those of the processes of the astrocytes of mixed type. On account of these facts, they are termed "dwarf astrocytes."

The monograph ends with a discussion of the morphologic and physiologic parallelism of the oligodendrocytes and the cells of Schwann. Although the oligodendrocytes of types I and II are different from the cells of Schwann, those of type III are more similar, while in the oligodendrocytes of type IV the similarity is complete. Between the first types of oligodendrocytes and the cells of Schwann there is a closely graded series of progressive stages in the organization of the perimyelinic sheaths. The structures found in the cells of Schwann are identical with the corresponding structures of the more differentiated oligodendrocytes. In both types of cells there are either fenestrated or reticulated membranous envelopes with fibrous and annular reinforcements, and scattered diaphragms or septums that break up the myelin column of the nerve fiber into a series of segments. The septums are probably continued around the axons as very thin sheaths.

The studies of several authors have shown that the cells of Schwann possess: (1) perinuclear cytoplasm continued around the myelin of the fiber as broad longitudinal bands and transverse, branched trabeculae (Cajal); (2) a system of more or less branched fibers in contact with the trabeculae mentioned (Nemiloff, Sanchez); (3) rings (Segall) connected with the fibers just mentioned by means of longitudinal trabeculae in contact with the edges of the clefts of Lantermann, or independent from these structures (Cajal), and (4) infundibular structures consisting of a spiral filament in relation with the clefts of Lantermann (Rezzonico, Golgi), or formed by a plexus of anastomosed filaments, mostly transverse, cemented together (Nageotte, Cajal). The fact that the four structures just mentioned have been disclosed with the aid of different methods has been the cause of their separate description by the authors.

The investigations of Hortega on the fibers of the central nervous system show that the sheaths and septums of these fibers corresponding to the clefts of Lantermann of the peripheral nerve fibers consist of the cytoplasm of oligodendrocytes in different stages of differentiation, and with somewhat different staining reactions. The latter account for the fact that in some cases only rings or infundibula appear stained, while in others the connections of these structures with the cytoplasm of the processes of the oligodendrocytes are clearly disclosed. And since the perimyelinic and endomyelinic organization of the central and peripheral fibers is similar, the conclusion that the reticula, fibers, rings and infundibula are differentiated parts of the cell of Schwann seems plausible.

The function of the oligodendrocytes, according to the author, is identical with the function of the cells of Schwann. The function of the latter has not yet been determined; while some investigators believe that the myelin of the fiber is lodged in the cytoplasm of the cells of Schwann under the form of inclusions, others affirm that myelin is formed by the neuraxon. Both hypotheses are surrounded by an array of facts, and the most important one in favor of the axonic origin of myelin is its degeneration on section of the fibers.

Sacristán has described cytoplasmic granulations similar in all respects to secretion granules in the cells of Schwann. The oligodendroglia also has well developed granular contents corresponding to the gliosomes of the astrocytes. Such granules are particularly abundant during embryonic development at that moment when myelinization of the nerve centers is at its height, and when growth of the nerve fibers is greatest in length and thickness. In the new-born cat the granules under discussion are abundant along the nerve fibers of the cerebrum, cerebellum and spinal cord. They are of variable size, and are arranged in irregular rows on the faintly stained processes of the oligodendrocytes. At a certain moment the granules seem to disappear, since the myelin sheath has developed and is also stained. One would be tempted to say that myelin arises through confluence of the granules, but this highly important point has not been demonstrated beyond reasonable doubt.

The indications of secretory activity on the part of the oligodendroglia suggest that the latter intervenes in the process of myelinization, but this intervention may be either direct or indirect. In the first case, adopted by Hortega as a working hypothesis, myelin would be a secretion of the oligodendrocytes, or, more exactly, an elaboration (incretion) of their cytoplasm with which it always preserves its relations. In the second hypothesis the oligodendrocytes would furnish the nerve fibers with the necessary trophic materials for the production of myelin.

The behavior of the oligodendrocytes during secondary degenerations is unknown, but the few facts revealed by a study of the encephalitis periaxialis of Schilder show that the oligodendrocytes do not remain unchanged when the nerve fibers disappear. The disappearance of the latter in the areas affected with the disease coincides with marked decrease in numbers and degenerative stages of the oligodendrocytes (mucoid degeneration). This suggests a close relationship between the two phenomena, but whether they occur simultaneously or independently is impossible to say.

In concluding, the author states that on account of the perimyelinic and endomyelinic organization of the oligodendrocytes they can be physiologically regarded as the cells of Schwann of the nerve centers. The true Schwann cells are to be regarded, on the other hand, as the oligodendroglia of the nerves. And, if logic does not fail, it must be supposed that the oligodendroglia and the cells of Schwann have the same blastodermic origin.

NONIDEZ, New York.

PROPRIOCEPTIVE BODY REACTIONS IN TOPICAL BRAIN DIAGNOSIS. Stephan Weisz, Ztschr. f. d. ges. Neurol. u. Psychiat. **118**:167 (Dec.) 1928.

The reflexes of Magnus and de Kleijn have been of great service in explaining many points in physiology. They are dependent on sensory stimuli, particularly those brought about in the changing positions of the head and body in space. The application of these reflexes to clinical studies has now begun, and Weisz reports a series of cases in which utilization was made of knowledge based on Magnus's researches.

The following phenomena were investigated especially in the cases reported: (1) Basic test, with arms extended to the front and eyes closed, and then active or passive movement of the head to the side as far as possible without pain. The head is held in this position. The arm toward which the chin is directed rises continually, the arms deviate chinward. This test is 90 per cent positive in normal persons, is much increased in cerebellar cases and is lacking in striopallidal-nigral disease. (2) Spontaneous rising reaction, consisting of a horizontal extension of the arms with the eyes closed, the arms rising continually, the right more than the left. This is positive in the majority of normal persons, and is increased on the side of the cerebellar disease. (3) Divergence reaction, consisting of a parallel extension of the arms in the horizontal plane with the eyes closed. The arms deviate without exception in the normal. (4) Convergence reaction, carried out in the same manner as the divergence test. The hands approach one another on flexing the elbows. This is not demonstrable in the normal, but is positive in striopallidal-nigral disease. (5) Pronation phenomena, consisting of an extension of the arms with the eyes closed, the volar aspect up. The thumb side of the hand is rotated upward. This is present without exception in normal persons, and increased in cerebellar and pyramidal lesions. (6) "Lagebeharrung," consisting of a horizontal extension of the arms, one arm remaining in this position, and the other, with the eyes closed, placed 60 degrees above or below the horizontal. After thirty seconds the patient is told to bring one arm up to the level of the other. The arm remains several centimeters above if placed originally above the stationary arm, or several centimeters below if placed originally below it. This is present without exception in normal persons. It is not present in striopallidal-nigral disease. (7) Imitation phenomenon, consisting of passive flexion of the leg, the other being brought to the same position. In cerebellar disease there is hyperflexion of the actively

moved leg. (8) Paradoxic deviation reaction, carried out with the same technic as test 1. In turning the head to the right the arms deviate to the left and vice versa. This may be unilateral or bilateral. It is observed in cerebellar disease. (9) Spontaneous rotation about the long axis, observed in cerebellar and parieto-occipital disease.

Weisz reports the cases of several patients in whom these various tests were employed. Case 1 was that of a man who had received a bullet wound in the right frontal region which was followed by pains in the head, attacks of vertigo and loss of memory. The Romberg test was positive, the fall being to the left and backward, and the gait deviated to the left. The postural reflexes showed an imitation phenomenon on the right, hyperflexion on the right and a tipping reaction to the left. Particularly interesting is the presence of the imitation of the sign which Hoff and Schilder up to now have found only in cerebellar disease. The hyperflexion was constant on the right, and was brought out only on imitation of the movement by the right leg. Weisz noted a new reaction in this case, namely, that if the patient stretched out his arms with the eyes closed, and locked his fingers in those of the examiner, one noticed that the tension in the left arm, at first gradually and then suddenly decreased, and at the same time the body tipped over to the left almost to the point of falling over. This was found frequently in frontal and cerebellar lesions, but never in pyramidal disease. Case 2 involved the left precentral convolution, with choked disks and a slight weakness of the right side of the face. It showed a positive tipping reaction to the right, a positive divergence and pronation reaction. Operation revealed a circumscribed swelling and edema in the transition zone between the frontal lobe and the precentral area. The neurologic signs, including the postural reflexes, disappeared after an operation.

Case 3 indicated a localized lesion in the zone between the frontal lobe and the precentral area. Neurologically, the right side of the face was weaker than the left, the tongue deviated slightly to the right and the right arm was somewhat weak. Of the postural reflexes, there was present a positive convergence reaction on the right, a lack of reaction on rotating the head to either side, a negative Lagebeharrung, stronger pronation on the right than on the left and no tipping reaction. The fact that there were epileptic fits (jacksonian) in this case, and that the encephalogram showed a lack of filling of the left ventricle indicated only part of the localization, says Weisz. On the other hand, the convergence reaction, the negative Lagebeharrung and the failure of the arms to respond to rotation of the head alone indicated involvement of the basal ganglia. This diagnosis was proved by an operation which showed an infiltrating tumor. The stronger pronation sign on the right is to be looked on as an expression of pyramidal disease in a stage in which hemiplegic symptoms were manifest only in the cerebral nerves. Thus in this case, by means of the postural reflexes, it was possible to make a diagnosis of involvement of the basal ganglia, the clinical signs indicating in addition an involvement of the frontal and precentral areas. Another similar case was reported in which on the basis of the postural reflexes a diagnosis of a right frontal lesion pressing on the basal ganglia was made. The positive signs were a convergence reaction only in the left arm, a bilaterally negative Lagebeharrung, a slight pronation reaction on both sides and a deviation to the left on rotation of the head.

In another case the clinical signs were obscure: past-pointing to the right with the left hand, a weak filling of the left ventricle by encephalogram and a high degree of choked disk. The only postural reflex present was a positive tipping reaction to the left. This was the only sign which indicated the true diagnosis, which was confirmed by necropsy.

The involvement of the pallidal system is indicated in the postural reflexes by a convergence reaction, a lack of response of the limbs to rotation of the head, and a negative Lagebeharrung phenomenon. These signs have been found in a few cases already quoted, and were found also in another case of paresis with pallidal involvement.

In two cases of involvement of the midbrain, the postural reflexes showed a positive convergence reaction, and a hyperflexion phenomenon—no imitation phenomenon.

The cerebellopontile angle cases were of interest. One of them showed an increased pronation tendency on the side of the lesion, a rotation of the trunk and sinking of the hand toward which the back of skull is turned on rotating the head to the right, a typical deviation on rotation of the head to the left, a positive imitation phenomenon, a sinking of the left arm on extension, together with an abduction of the lowered arm. The tumor at operation was found to extend beyond the midline, thus giving rise to the right-sided signs. In a right angle tumor there was a positive imitation phenomenon on both sides, hyperflexion, a tipping reaction to the right, an increased convergence reaction and a markedly positive Lagebeharrung. The latter has been observed by Schilder in such a case. In still another case of right angle tumor there were positive hyperflexion, imitation and tipping reactions all to the right.

The cerebellar cases all showed a positive imitation phenomenon and increased pronation signs on the side of the lesion. In a case of hereditary ataxia (cerebellar) the imitation sign was present on both sides.

Weisz says that these postural reflexes are of definite value in localizing the side and site of a cerebral lesion. The most important tests in this connection are the imitation phenomenon, the tipping reaction and the pronation sign. The imitation and tipping phenomena are signs of a homolateral cerebellar or heterolateral disease of the frontal lobe. The pronation sign is increased in homolateral cerebellar lesions as well as on the side of pyramidal tract involvement. The divergence reaction is increased usually on the side of cerebellar injury. The convergence reaction is a contralateral sign but its latency and course must be followed in relation to the other arm always. In addition, the course of certain reactions is influenced by the different sites of lesion, as for example, the protracted, slow, discontinuous convergence reaction in pontile cases, as well as the sinking of the limb toward which the base of skull is turned in rotation of the head away from the lesion in pontile angle cases, and the positive Lagebeharrung phenomenon in cerebellar cases. Weisz is definite that these reactions are of great value in the topical diagnosis of cerebral disease.

ALPERS, Philadelphia.

A STUDY OF INTRACRANIAL SURGERY. HUGH CAIRNS. Published by the Medical Research Council, London, 1929. Special Report Series, no. 125.

Under the aegis of the Rockefeller Foundation, a young neurologic surgeon was sent from England to the United States to prepare a report on neurologic surgery as practiced in the United States, with special reference to the work in the Brigham Hospital, Boston. Such a report is obviously difficult to prepare and on reading it one is at once impressed by the high praise given unstintedly to the progress of technical operative procedure in the United States. Criticism of this unstinted praise appears in the *British Medical Journal*, where the writer's attention is called to the fact that the early work of the English pioneers laid the foundation for this brilliant progress in technical details and methods. The writer of the report defends himself from such criticism by pointing out that he reported facts as he saw them. Such defense, although ingenious, is not sound, for any critical report to be of real value must of necessity be based on an extensive knowledge of the subject and its development in different countries. Here, criticism might in turn be directed against the critic in the *British Medical Journal*, for not only has the work of the English pioneers importance but also the work of French, German, Dutch and investigators of other countries holds an important place in the development of neurologic surgery. As in anatomic and physiologic work, so in neurologic publications a high standard of scientific probity is essential. The report is limited to a description of the treatment for cerebral tumors. Such tumors present peculiar and grave difficulties to the neurologic surgeon. They are unlike new growths in other parts of the body and demand special treatment.

Too often the surgeon has to be contented with a palliative operation whereby he may conserve vision or secure for his patient a few more years of life. Indeed, such partial results are often to be considered as very good. In cases in which it is possible to remove a whole cerebral tumor, such removal has frequently to be performed in several sessions, necessitating repeated precautions and tedious operations. Cushing, for example, after an operation lasting from three to five hours, left his patients on the table until they regained consciousness. All sorts of factors serve to complicate cerebral surgery, as is abundantly manifested in cases of tumor in the roof of the fourth ventricle. Here it would be technically easy to remove the tumor, but removal would cause such lesions to the vital centers in the fourth ventricle that death would immediately supervene. Again, should the tumor lie in the motor zone it is easily exposed and if encapsulated might be removed as readily as an ovarian tumor, but here again profound hemorrhage would almost certainly cause the death of the patient. Should he escape this fate, the destruction of the surrounding brain tissue caused by the removal of the tumor would cause almost certainly paralysis with probable loss of speech.

With such dangerous complications in view it is obvious that an intracranial operation cannot be undertaken lightheartedly. Every known mode of diagnosis and localization must be carefully applied and every precaution taken to ensure at least a palliation of the symptoms and safety to the patient.

It is interesting to note in the report that the writer was less impressed by the progress of new methods of diagnosis and of technic (the roentgen rays, air inflation, coagulation) than by the fact that when an incorrect localization has been made it is always due to the wrong interpretation of old diagnostic points. This observation certainly suggests that greater attention must be paid to older diagnostic points, and further that operation should be insisted on before irreparable complications have appeared, more particularly those affecting the eyesight.

In the United States, as in Europe, 10 per cent of brain tumors come to the neurologic surgeon when the eyesight has gone. Is there here not material for grave thought, not so much for the general physician as for the aurist, the rhinologist and the ophthalmologist? These specialists see many of the patients before cerebral tumor is suspected. It certainly appears that more consideration should be given to the possibility of cerebral tumor. The opening of the antrum, removal of a concha or the modification or strengthening of the lenses is not always the correct line of treatment, although it may be indicated by the patient's immediate symptoms; the possibility of cerebral tumor should never be forgotten.

An accurate observation made in the report is that the neurologic surgeon must be able to diagnose his own cases, independently from the neurologist, for as a surgeon he has to consider factors which would not appeal to a pure neurologist. For example, it may not be of great importance for the neurologic surgeon to know whether the tumor lies in the anterior or the posterior central convolution, for the same flap exposes both areas, but it is of importance to know how the tumor has developed, as the choice of the flap formation depends on this detail.

It is interesting to read the report on the use of air inflation for localization. Several striking examples are given in which this method has caused serious complications, but the writer concluded that when all other methods of localization are impossible (this is not common now) air inflation is of value in diagnosing the position of a tumor on the right or the left side of the great brain.

In connection with this point it appears from the report that the correct proportion of time to be spent in the clinic, the operating theater, the library and the laboratory has not yet been reached in America. For example, on page 40 of this report, one finds the dangerous diagnostic method of air inflation (mortality, 10 per cent) applied in a case whereas the patient, with a surely supratentorial tumor, tended to fall to the right and backward. For fifteen years it has been known that in such a case the tumor must be situated in the left hemisphere and involves the corpus striatum.

Some interesting details regarding hemorrhages, hyperthermy and other complications conclude this most interesting booklet.

MUSKENS, Amsterdam.

ETIOLOGIC FACTORS OF EPILEPSY IN CHILDREN. T. P. SIMPSON, Collected Papers, Psychiatric Clinic, First Moscow State University **3**:274, 1929.

The author studied 296 children who were referred to the clinic for convulsive disorders conducted by the Moscow Board of Health. Most of the children were under the age of 3. One hundred and twenty were found to be suffering from spasmophilia or allied conditions. The author differentiates spasmophilia from epilepsy and gives her diagnostic criteria. Spasmophilia manifests itself in asphyxia due to a laryngeal spasm or to other causes. It is bilateral and is usually not followed by loss of consciousness and sleep. The attacks usually come on during the day and have a relationship to some psychogenic factor such as fright, punishment, etc. After the age of 2, spasmophilic attacks cease. The intellectual development of such children is normal. Epileptic seizures are observed in children of all ages; they come on very often without special cause. The seizures begin often during sleep, are at first unilateral, are accompanied by loss of consciousness and are followed by deep sleep. These attacks often leave some neurologic residuals, and parallel with this there is intellectual retardation of the child, with marked personality change and often a complete alteration of the psyche.

In describing the spasmophilic conditions, the author states that the attack would either stop during the tonic convulsion of the whole body or would go on to clonic convulsions with loss of consciousness and light reflex and involuntary micturition and defecation. Quite often the first attack occurred during the course of an infection with high fever; then it would recur under psychic stimuli and would thus appear to be functional in origin. Once equilibrium is disturbed, comparatively insignificant factors may give rise to a seizure. The personality of children with spasmophilia shows a tendency toward marked irritability, restlessness, aggressiveness and, at times, rather antisocial behavior.

One hundred and seventy-six children had rather definite epileptic seizures. The ages in this group varied from infancy to 14. Hereditary factors were present in more than half of the cases. In 104 of these cases one could trace a definite organic etiology; 4 children had an endocrine toxic epilepsy, and in 68 cases no etiologic factors could be ascertained. In the first group of 104 children, encephalographic studies were made by the lumbar route; in about half of these children some definite pathologic condition of the brain, such as residuals of encephalitis, trauma, cortical atrophy, etc., was observed. In a few cases, there were systemic intoxications such as uremia, enteritis and nephritis. In 5 cases, intestinal parasites were the only thing discovered which could account for the attack. The author calls attention to a large number of minor neurologic signs found in these children.

The aura consisted often of visual hallucinations. The personality change consisted in the appearance of either sadistic or masochistic trends, with the development of what Jones has described as homosexual character traits such as meticulousness, accuracy, stinginess, etc. While the adult epileptic patient is usually sluggish and somewhat ponderous, the epileptic child is very restless, noisy and somewhat hypomanic. In epileptic children one observes tremendous resentment toward authority with severe temper outbursts when crossed.

In the cases of nineteen children, intra-uterine infections and toxins played an important rôle. There was either syphilis or alcoholism of one or both parents. The author calls these cases constitutional epilepsy. In these cases the attacks developed soon after birth and the children were extremely difficult to handle on account of severe temper tantrums. The author calls these children congenital psychopathic patients.

The author comes to the conclusion that encephalography is an extremely important aid in studying epilepsy in children. It very often reveals marked pathologic changes of the brain, even when a neurologic examination gives absolutely negative results. The etiology of epilepsy is extremely complex, but given a constitutional predisposition to convulsive manifestations, slight toxic factors may elicit the seizures. A thorough study of all factors involved, metabolic, psychic and neurologic, will help to narrow down the extremely large groups of the idiopathic epilepsies.

KASANIN, Boston.

REPORT OF BRITISH PSYCHO-ANALYSIS COMMITTEE. Suppl. Brit. Med. J. **1**, June 29, 1929.

As the result of a motion made at the annual representative meeting of the British Medical Association, at Nottingham, in 1926, a special committee was appointed by the Council of the British Medical Association "to investigate the subject of psychoanalysis and report on the same." This committee, numbering about twenty, composed not only of leading psychiatrists but also of leading British representatives of other specialties such as orthopedics, ophthalmology and obstetrics extended its meetings from March, 1927, until May, 1929.

The elaborate report includes: (1) An historical survey. (2) A consideration of psychoanalytic methods and teachings. (3) An examination of other analytical methods, which includes a detailed statement furnished to the committee by a prominent exponent of Jung's work and a brief consideration of the deviations of Stekel, Adler and Rank who claim to have inaugurated distinct schools of thought. (4) The scope of psychotherapy. (5) Misconceptions concerning psychoanalysis and the attitude of psychoanalysts to criticism.

The conclusions are as follows: I. Psychoanalysis is a term now used in two ways: (1) in a loose popular sense hardly capable of description or definition so wide is its extension; (2) in the strict sense of the technic devised by Freud, who first used the term, and the theory which he has built on his work. It is accordingly recognized that in any scientific enquiry into the matter the claims of Freud and his followers to the use and definition of the term are just and must be respected.

II. It is recognized that there are workers and writers of repute in the field of psychology and psychopathology who use an exploratory therapy but do not claim to be psychoanalysts, and indeed adopt some other descriptive term such as analytical psychology, individual psychology, deep mental analysis, etc., and, further, that there are practitioners of other methods of psychotherapy, hardly, if at all, connected with any recognized form of analytical teaching, to whom the term psychoanalyst is also often quite wrongly applied by the public. The committee recognizes that psychoanalysis should not be held responsible for the opinions or actions of those who are not in the proper sense psychoanalysts.

III. The committee has recognized certain other misconceptions in relation to psychoanalysis, and has endeavored to remove them.

IV. The committee finds that even among many of those most hostile to psychoanalysis there is a disposition to accept the existence of the unconscious mind as a reasonable hypothesis, though some prefer to use other terms to describe what is meant. Some members of the committee, however, do not even go so far as this.

V. The committee has set forth the most important of the criticisms of the theory and method of psychoanalysis, together with the answers of a recognized psychoanalyst (Dr. Ernest Jones) thereto. It is the opinion that it is impossible for the committee to make any general pronouncement on questions of this nature.

VI. From the nature of the case, the committee has had no opportunity of testing psychoanalysis as a therapeutic method. It is therefore not in a position to express any collective opinion either in favor of the practice or in opposition to it. The claims of its advocates and the criticisms of those who oppose it must, as in other disputed issues, be tested by time, experience and discussion.

OBERNDORF, New York.

PATHOLOGIC CHANGES IN THE CORTEX IN TUBERCULOSIS AND EARLY PSYCHIC INVALIDISM. V. C. STEFFKO, Collected Papers, Psychiatric Clinic, First Moscow State University **3**:126, 1929.

In studying his material, the author paid special attention to the previous occupation of his patients. Thirty-seven brains were studied and subdivided into three groups. In the first group of twelve cases, the brains belonged to people who were engaged in intellectual work. In the second group of eleven cases, the brains belonged to people who were manual workers but who suddenly, on account

of the revolution, were given positions requiring a great deal of intelligence and responsibility. In the third group, the brains belonged to people engaged in simple manual work. All the patients died from pulmonary tuberculosis. The brains in the first and second groups showed a large number of minute adhesions of the dura as well as of the pia and the arachnoid in the region of the vessels. These adhesions were found mostly in the frontal lobes and were about from 2 to 3 mm. in diameter. A microscopic examination of these areas showed that the brain coverings were adherent to the adventitia of the pial vessels. Together with this one could see small hemorrhages, which consisted of migrations of red blood corpuscles by diapedesis with connective tissue proliferation. The outer wall of the pial vessels was often thickened, forming an aneurysm-like convexity. The blood vessels showed a hyaline degeneration with marked sclerosis leading to endarteritis obliterans. Some of the smaller vessels were completely obliterated.

In the study of the cellular pathologic changes the important thing noticed was the shrinking of the pyramidal and ganglion cells in the third layer of the cortex. There was also marked sclerosis of the ganglion cells, the term being used in Spielmeyer's sense. The degenerative changes in the cells consisted in the deposit of fatty pigments and the precipitation of basophilic granules. In the cortex, small areas of neuroglial proliferation and islands of spongy tissue were also noted. These changes have been described by other pathologists in some acute and severe toxemias.

The most significant pathologic changes were found in the second group of patients who were engaged in highly specialized work for which they were not prepared and which was beyond their ability. In this group, microscopically, there were some edema of the brain and many soft spots. As tuberculosis as such produces very little change in the central nervous system, the author believes that the emotional and intellectual strains to which these persons were subjected was responsible for the appearance of the early sclerotic changes in the brains. What one saw was really a premature aging of the brain cells on account of their special vulnerability due to previous toxemias and infections. Many of these patients had been starved, and about 50 per cent of them had had typhoid fever as well as typhus. As the patients in the second group showed the most pronounced changes in the central nervous system, the author comes to the conclusion that prolonged and unusual emotional and intellectual strain results in the early appearance of arteriosclerosis in the brain. This goes parallel with the conclusions reported by Gannushkin in his description of a new clinical syndrome of early psychic invalidism.

KASANIN, Boston.

CONGENITAL AUDITORY IMPERCEPTION (CONGENITAL WORD-DEAFNESS): WITH REPORT OF A CASE. C. WORSTER-DROUGHT and I. M. ALLEN, J. Neurol. & Psychopath. **9**:193 (Jan.) 1929.

Congenital word-deafness is a rarity, and its inevitable disorganization of speech mechanisms has often led to misinterpretation of the underlying defect. A case is presented in detail in which the outstanding defect is the inability to appreciate the significance of spoken words; but, in addition, there is also considerable inability to distinguish between less specialized sounds. The authors therefore suggest the new term, "congenital auditory imperception," to cover this condition for which "word-deafness" is too limited. It was evident early in this case that there were no defects in the peripheral organs of hearing and sight, and still less in the muscles of articulation and expression. At the age of 5, the patient went to a deaf and dumb school and learned some lip reading. Only after this did he use any words spontaneously. The authors recognize the futility of trying to place the different parts of the speech mechanism in separate and clearly defined "centers"; they accept the complete interdependence of each speech element, but consider it desirable, for simplicity in discussion, to use the old term "center" without implying the existence of a definite anatomic unit. In the absence of a "word memory center" it is evident that, with the perfection of lip reading, the

boy will have to build up, from his memories of lip movements and facial expressions and their association with persons, objects and affective states, a new "center" for the memory of words which may be called the "lip reading word-memory center." This has been partially accomplished. There has been developed in this case a method of expression which is of the nature of so-called "idioglossia"—an individual language representing an extreme form of mispronounced and ill expressed conventional language. As regards causation, the balance of evidence is in favor of a biologic variation or of local aplasia, but birth injury cannot be definitely excluded. Important questions grow out of this type of case such as the influence of this defect on general intelligence, the resulting abnormal psychology, the relation to delinquency and the importance of special educational methods to bring such patients to a self-supporting status.

FAVILL, Chicago.

DEMENTIA PRAECOX AS AN ENDOCRINOPATHY WITH CLINICAL AND AUTOPSY REPORTS. JOHN LINCOLN MCCARTNEY, Endocrinology **13**:73 (Jan.-Feb.) 1929.

The author has made a study of twenty-three eunuchs who, he concluded, showed evidence of typical dementia praecox or of schizoid characteristics. The patients were intelligent and apparently normally oriented but had distinct changes in affect. A few of these patients had retained sexual function but without libido. Because of these observations the author decided to study a series of schizophrenic male patients and concluded that at least 60 per cent were definitely eunuchoid in type; only from 5 to 6 per cent had normal genital organs, but they showed other signs of endocrine dysfunction. He also examined forty living female subjects with dementia praecox and of these 52.5 per cent had unquestionable ovarian disease although some of these patients had been pregnant. Postmortem examinations were made of 158 male and 24 female schizophrenic patients. Many of them showed marked endocrine changes. The endocrine changes, however, were not consistent except as regards the gonads and suprarenal glands. The thyroid was normal or hypertrophied in all cases of catatonic dementia praecox. In none of the female schizophrenic patients were normal ovaries found, and in only a small percentage of the males were normal testes found. The author concludes that sex activity and fecundity are not adequate criteria of gonad incretion; rather he believes that the state of interstitial lipoid should be taken as the criterion of normality and that, from the study, it is indicated that dementia praecox is primarily an endocrinopathy in which the gonads are constantly at fault. It is interesting to note that tuberculosis was the cause of death in about 40 per cent of the men but in only 15 per cent of the women, and that in almost every case of dementia praecox there was a history of one or more of the severe toxemias.

WAGGONER, Ann Arbor, Mich.

MAJOR HYSTERIA WITH ATTACKS OF IMPAIRED CIRCULATION OF THE LEFT UPPER LIMB. W. G. SPILLER, J. Neurol. & Psychopath. **9**:113 (Oct.) 1928.

A boy, aged 19, who had received a blow on the head followed by coma for two hours, subsequent headache and syncope, developed numbness and swelling of the left arm. This lasted six weeks. Four months after the original injury, he was hit on the head by a baseball. The next day he fell unconscious while at work and again had headache. In the next ten months he was well except for attacks of swelling of the left arm which would become purplish and cold from the elbow down. He next had an attack of headache and syncope for several hours without convulsion. As he was regaining consciousness he had muscular twitchings over the whole body. Similar twitching attacks followed, with opisthotonus but with no biting of the tongue or incontinence. They lasted one minute and were frequent. The pupils were dilated but reacted slightly to light; the attacks were typically major hysteria. Laboratory and roentgen examinations gave negative results. Later attacks occurred with the patient lying on his right side and the

left arm more violently extended along or a little behind the trunk. The reddish purple cyanosis appeared in the whole left arm. The blood pressure was less on this side during this condition, and at times no pulse was detectable. Suggestion failed to produce the attacks of cyanosis but did influence the convulsions. Consideration is given to the possibility that a hemorrhagic thalamic lesion from the head trauma was responsible for the abnormal vasomotor phenomenon. The more probable explanation is a mechanical one, contraction of the adductors of the shoulder or isolated contraction of the scalenus anticus muscle compressing the subclavian artery.

FAVILL, Chicago.

THE INCIDENCE OF INTRACRANIAL TUMORS WITHOUT "CHOKED DISK" IN ONE YEAR'S SERIES OF CASES. WILLIAM P. VAN WAGENEN, Am. J. M. Sc. **176**:346 (Sept.) 1928.

In a series of 145 patients with verified intracranial tumors, seventeen, 11.7 per cent, failed to show the presence of a choked disk at the time of admission. Albutt, in 1871, was one of the first to observe that a brain tumor occurred in the absence of choked disk. Of the seventeen verified tumors without choked disk, six of the tumors occurred in the posterior fossa; three were acoustic neurinomas, two were cerebellar and one was medullary. In three of the cases hydrocephalus was present. There were eleven tumors above the tentorium and none were associated with hydrocephalus; six were temporal or supramarginal, four parietal and one parasagittal. The absence of choked disk in tumors does not mean that increased intracranial pressure does not exist, for in 50 per cent of the cases there was evidence of increased tension, such as hydrocephalus, flattening of the convolutions or protrusion of the brain after decompressive measures.

In 30 per cent of the cerebral tumors, both verified and unverified, without choked disk, calcification was demonstrated by the roentgenogram. The author reviews the theories in regard to the mechanism of choked disk. He leans toward the view that there is interference with cerebrospinal circulation by the tumor either by position or by accompanying edema.

MICHAELS, Detroit.

DEMENTIA PARALYTICA: THERAPEUTIC MEASURES AND RESULTS. ARTHUR POOL, J. Neurol. & Psychopath. **10**:21 (July) 1929.

The malarial treatment for paresis was commenced at the County Mental Hospital, Rainhill, in June, 1923, and, since March, 1927, tryparsamide has been used in addition. The total admissions from January, 1923, to December, 1928, were 274. Of these, 182 patients have died, 51 are still resident and 41 have been discharged as "cured." This paper is a detailed study of the after-histories in the "cured" cases. It was possible to keep in touch with 30 of the patients. Of these, one died of an intercurrent disease and three of paresis, four have been readmitted to mental hospitals and twenty-two are alive and enjoying normal mental health. The author concludes that malaria alone is as effective as the combined therapy in producing a remission of mental symptoms and changes in the serologic reactions. Tryparsamide is an important adjunct to malaria, acting as a general physical tonic, allaying motor restlessness and thus making subsequent nursing through the pyrexial attack easier and less fraught with danger to the patient. It is apt to induce serious complications, the more important being visual defect and hepatic upset. The drug should therefore be used cautiously and adequate safeguards and controls should be employed. The word "cure" being defined as a complete remission of mental symptoms, serologic changes and accompanying physical signs, no case recorded in this series can be said to have been completely cured. If one is ever to record a complete scientific cure of paresis it will come from effectively following up these cases after discharge from lunacy certification, so that the ever-present syphilitic factor can be adequately treated.

FAVILL, Chicago.

EPIDEMIC ENCEPHALITIS IN BURJATIO-MONGOLIANS. BERINGER, J. f. Psychol. u. Neurol. **39**:254, 1929.

The author had occasion to observe ten cases of epidemic encephalitis in the Burjatio-Mongolian republic. Four of the cases occurred among the Russian population and six among the Burjations. They were all late cases and parkinsonian in type. Two of the patients traced their illness back to 1920, one to 1921, four to 1923, and three could not remember when they became ill. The onset of the illness (in those cases in which it could be determined) was always in the winter or early spring. The clinical picture resembled that observed during the epidemics in Germany. Most of the cases showed fever, diplopia, myoclonic twitchings and sleep disturbances (either excessive sleep or sleeplessness). The first symptoms of involvement of the extrapyramidal system, such as akinesia, tremor and rigidity, made their appearance in the second year of the illness and gradually progressed to severe parkinsonism with masked facies, loss of associated movements, most intense rigidity, marked tremor, propulsion and retropulsion, encephalitic speech disturbances and salivation. At the time of examination, the ages of the patients were as follows: among the Russians, 27, 28, 28, 37; among the Burjations, 35, 37, 38, 46, 47, 50 (?). Most of the cases were typical, except one which the author describes in great detail because the patient had, in addition to cranial nerve and extrapyramidal involvement, compulsions and generalized epileptiform convulsions.

KESCHNER, New York.

TUMOUR OF THE BRAIN, ASSOCIATED WITH DIFFUSE SOFTENING AND TURBID CEREBROSPINAL FLUID: REPORT OF A CASE. HARRY L. PARKER, J. Neurol. & Psychopath. **10**:1 (July) 1929.

A man, aged 58, previously well, suddenly developed difficulty of speech and weakness of the right hand and arm. In two weeks he had lost voluntary speech and had a right hemiplegia. The blood pressure was 125 systolic and 80 diastolic. There was no edema of the optic disks. Under observation, the temperature soon rose to 102 F. and stupor developed. The spinal fluid was greenish yellow, with 1,600 polymorphonuclear leukocytes but no visible organisms and no growth on culture. The original diagnosis of thrombosis of the left middle cerebral artery was questioned because of the spinal fluid observations, and a left subtemporal decompression was done. The brain appeared flattened and softened with no evidence of increased intracranial pressure. Death occurred in twenty-four hours. Necropsy showed a small tumor, 5 cm. in diameter, in the tip of the left temporal lobe. It reached the inferior horn of the left lateral ventricle. There was extensive softening. The left middle cerebral artery had no thrombus but could easily have been compressed by the tumor. The high spinal fluid cell count resulted from invasion of the lateral ventricle. The pathologic diagnosis of the tumor was spongioblastoma multiforme. The case illustrates the difficulties which may arise in differentiating tumor, thrombosis and inflammatory cerebral disease.

FAVILL, Chicago.

A PECULIAR FORM OF A HEREDOFAMILIAL DISEASE. M. Y. SEREYSKY, Collected Papers, Psychiatric Clinic, First Moscow State University **3**:201, 1929.

The author describes a new form of a hereditary familial disease which he has observed in three brothers and one sister. All were young, aged from 20 to 30, and presented a late development of speech with defective hearing. All began to talk at about the age of 4. On physical examination, the important things noted were: all had night blindness with definite retinitis pigmentosa, nerve deafness, dysarthria and mental deficiency. In addition, the author noted marked vasomotor instability, under-development of secondary sexual characteristics, lack of energy, sluggishness and sexual infantilism. The family history was without significance as far as could be ascertained. Both parents were in good health. The mother had had

twelve pregnancies; seven of the children were living, four of whom had the symptoms described. Metabolic studies showed very little out of the way, and the Wassermann reaction of the blood and cerebrospinal fluid was negative. It is interesting that the nerve deafness involved only the cochlear and not the vestibular apparatus. The dysarthria consisted in an inability to pronounce certain consonants and a monotonous quality of the voice. Neurologic examination gave essentially negative results. The sella turcica showed no changes. Encephalography showed no disturbance of the ventricular system. The author believes that these cases have some relationship to delayed forms of amaurotic family idiocy, described recently by Schaeffer, and also perhaps to the Biedl-Bardet syndrome.

KASANIN, Boston.

SYRINGOMYELIA: A CASE REPORT WITH DISCUSSION AND DIFFERENTIAL DIAGNOSIS. B. LANDIS ELLIOTT and D. F. HOGAN, J. Nerv. & Ment. Dis. **70**:129 (Aug.) 1929.

Morvan was the first to describe the condition of painless felons on the fingers with ulceration and necrosis of the terminal phalanges. Cavities in the spinal cord were found at autopsy and Morvan's disease is now considered as a variety of syringomyelia. The dissociated sensory phenomena, thermanesthesia and analgesia with retention of tactile sensibility, are due to interruption of the posterior gray commissure and the lesion is most frequently found in the lower cervical and in the upper three thoracic segments.

The authors report in detail the case of a man, aged 61, who showed a painless infection and necrosis of the left hand, which began in the distal phalanx of the left index finger. An infection that had followed a trauma on the right hand had resulted, three years previously, in amputation of the arm below the elbow. The patient had a spinal concussion when hurled from a hand car twelve years before. His pupils showed a paradoxic reaction to light, and they dilated gradually through a small arc on illumination. Cervical ribs, progressive muscular atrophy, leprosy, neurosyphilis, and Charcot's joints were ruled out by differential diagnosis. Although syringomyelia is usually regarded as congenital in origin, Fuchs, Oppenheim and Kienboeck established the causal relationship between syringomyelia and trauma. The case described illustrated this relationship.

HART, Greenwich, Conn.

CONGENITAL AUDITORY IMPERCEPTION (CONGENITAL WORD-DEAFNESS): INVESTIGATION OF A CASE BY HEAD'S METHOD. C. WORSTER-DROUGHT and I. M. ALLEN, J. Neurol. & Psychopath. **9**:289 (April) 1929.

The investigation of a case of congenital auditory imperception by Head's method is described in detail. In a previous communication describing the case, word-meaning deafness was shown to be the most important element of the defect, but some degree of word blindness and agraphia was demonstrated as well as a pronounced speech defect of the nature of so-called idioglossia. In order to distinguish between the patient's actual word hearing and his ability to lip read, the method was varied in one particular from that employed by Head for the investigation of cases of aphasia. Each test is shown in tabular form and the capacity and defects of the patient both on the "receptive" and "executive" sides are summarized. The deficient background of congenital aphasia is contrasted with that of acquired aphasia, and an estimate is made of what the patient has been able to acquire in the form of language. This application of Head's method disclosed rather more than the ordinary routine method and emphasized more definitely the salient features of the disorder. It is doubtful if Head's method will prove of value in congenital aphasia, as, in the majority of such cases, means of communication with other individuals is so imperfect and the background of knowledge so deficient that any method of approach has of necessity to be very simple.

FAVILL, Chicago.

THE PRODUCTION OF GENE MUTATIONS BY ROENTGEN RAYS. N. W. TIMOFÉEFF-RESSOVSKY, J. f. Psychol. u. Neurol. **39**:432, 1929.

In 1927, H. J. Muller published the results of experiments on the effect of roentgen radiation on the genovariability of *Drosophila melanogaster*. He found that in this manner the "normal" rate of gene mutation could be raised more than a hundred-fold. This increase in rate was by no means specific for *Drosophila melanogaster*, but producible also in plants (barley, maize and tobacco), in *Vespa harboracon* and in another variety of *Drosophila; Prosophila funebris*. It would seem from all the experiments undertaken thus far that short-wave rays are most effective. It would also seem that the different mutations produced by radiation depend on the structure of the individual genes. Other experimenters employing the same methods found that in some cases the mutation of genes is a reversible process.

The practical significance of this work by Muller and his co-workers is merely that by means of roentgen radiation mutation of genes can be hastened. By utilization of this method in the cultivation of plants, it will probably be possible in the near future to produce new species of plants. As far as human beings are concerned, Muller's discoveries will have to be borne in mind whenever a human being is subjected to irradiation by roentgen rays, because lethal or pathologic manifestations may follow such irradiation, which it will not be possible to obviate by selection.

KESCHNER, New York.

UNUSUAL SENSORY PHENOMENA FOLLOWING REMOVAL OF A TUMOR OF THE SENSORY CORTEX. I. M. ALLEN, J. Neurol. & Psychopath. **9**:133 (Oct.) 1928.

A detailed description is given of a case of meningioma of the postrolandic sensory cerebral cortex with operation and subsequent abnormal stereognostic phenomena. These consisted in: (1) spontaneous sensations of the presence of solid objects in the affected hand; (2) sensations of the presence of solid objects in the affected hand when they were actually present and felt in the unaffected hand, and (3) persistence of the sensations of the presence of objects in the affected hand for an appreciable interval after they had been removed therefrom. The probable causes of these phenomena are discussed as follows: (1) the effect that accidental positions of the affected hand might have in the production of spontaneous stereognostic sensations; (2) the effect that local impulses, arising in the sensory structures immediately above the thalamus, as a result of post-operative circulatory changes in that region, might have in the production of spontaneous "formed" sensations, in contrast with the effect of lesions of, or close to, the cerebral cortex in the formation of spontaneous "unformed" sensations, and (3) the effect that postoperative mental fatigue might have in the misinterpretation of the local sensory impulses arising at the suprathalamic level. The second explanation is favored.

FAVILL, Chicago.

THE ENCEPHALITIC PSYCHOSES. E. TOULOUSE, L. MARCHAND and P. SCHIFF, Encéphale **24**:413 (May) 1929.

Six cases are described which came to autopsy; all the patients except one were in the third decade of life and presented a varied symptomatology in the psychic sphere. Anxious depression, catatonia, delusions of reference and acute confusion were the outstanding pictures. Clinically, they were simple psychoses without fever or signs of neurologic localization, but in each case a period of hyperthermia occurred before death. They are considered as the clinical expression of a type of meningo-encephalitis characterized by acute cellular changes (chromatolysis, eccentric displacement of the nucleus and hyaline changes) in the central ganglia and the cortex, by vascular inflammatory lesions and by the presence of infectious nodules, variously located but especially in the bulb and the central nuclei. These nodules are probably glial formations arranged in rosets or nodules; evidence is presented that they are the cause of the hyper-

thermia and not the result. There is considerable discussion of the present impossibility of separating the various types of encephalitis on the basis of the etiologic agent. But the most important point appears to be that here is a series of cases, which would generally be considered as nonorganic or functional, later proved by neurologic localization and by pathologic examination to be strictly organic types.

ANDERSON, Los Angeles.

MICROGLIA: AN EXPERIMENTAL STUDY IN RABBITS AFTER INTRACEREBRAL INJECTION OF BLOOD. E. A. CARMICHAEL, J. Neurol. & Psychopath. **9**:209 (Jan.) 1929.

One half cubic centimeter of blood withdrawn from a rabbit's ear vein was injected into the brain substance of the same rabbit under ether anesthesia. Fifteen rabbits were so treated and killed at intervals of from one to twenty-two days. The head was immediately perfused with physiologic solution of sodium chloride through both carotids or the arch of the aorta, followed by a formaldehyde bromide mixture before removing the brain. Using a special staining technic, the author drew the following conclusions: Microglial cells are the chief elements concerned with the phagocytosis of damaged brain tissue and in part with the removal of red blood corpuscles lying free in the brain substance. Large mononuclear cells, probably derived from the reticulo-endothelial system, are also concerned with the removal of red blood corpuscles. Microglia cells commence to remove products of degeneration within a few hours of wounding. Microglia cells may engulf red blood corpuscles in the early stages and contain pigment in the later stages. Astrocytes degenerate rapidly and only commence to recover and to wall off the wound at the end of five days. Astrocytes do not act as phagocytic agents. Red blood corpuscles may remain as such in the cerebral tissue for not longer than twelve days.

FAVILL, Chicago.

A CASE OF THOMSEN'S DISEASE. PIERRE HOFF, Encéphale **24**:260 (March) 1929.

A case of this relatively rare malady is described. The first symptoms came on in 1916, when the patient found himself unable to relax an object held in his hands. This continued intermittently until he came under the observation of the writer in 1928. A large number of the muscles, including those of the arms, thorax and abdomen, would go into tonic contracture when he voluntarily innervated them. Particularly was this the case with the muscles of the fingers and toes. The eyes could be opened and closed without difficulty, and even in attacks there was no loss of reaction. Pain reactions accompanied the contractures, which lasted for from seconds to minutes. Tendinous and cutaneous reflexes were normal, as were the various forms of sensation. Spinal fluid pressure was greatly increased, being 42 mm. of mercury in the horizontal position. To the faradic and galvanic currents, the nerves and muscles evidenced hyperexcitability.

ANDERSON, Los Angeles.

LEBER'S OPTIC ATROPHY AND ITS RELATIONSHIP WITH THE HEREDO-FAMILIAL ATAXIAS. FERGUS R. FERGUSON and MACDONALD CRITCHLEY, J. Neurol. & Psychopath. **9**:120 (Oct.) 1928.

The purpose of this paper is to draw attention to the existence of an atypical variety of Leber's disease, wherein positive neurologic signs were present in addition to optic atrophy. One member of the family of four showed epilepsy and mental defect, while another showed features of pyramidal disease, nystagmus, ataxia and sensory loss. This family represents a probable transition type between Leber's disease and Marie's ataxia and tends to support Raymond's unitary conception of heredofamilial diseases of the nervous system. The association with neurologic disturbances may contribute to knowledge of the etiology of Leber's

disease by suggesting that the essential pathogenic process is a neuronic abiotrophy, limited — in typical cases — to the optic nerve. The presence of neuritis in the early stages may be explained as the result of toxic products of degeneration or the optic nerves may be inherently vulnerable but require the intervention of some added factor, such as near-by sepsis, to develop neuritis and consequent atrophy.

FAVILL, Chicago.

PYRETOTHERAPY IN SCHIZOPHRENIC HALLUCINOSIS. A. VALLEJO NAGERA and P. A. NOUVILLAS, Arch. d. neurobiol. **8**:273 (Nov.-Dec.) 1928.

This article is a report on the effects of antityphic vaccine on six patients suffering from schizophrenic hallucinosis. The injections were made intravenously, and after several trials it was found that three injections a week produced a rise in temperature reaching 40 C. (104 F.). The first injection was of 200,000,000 of bacilli, followed by injections as high as 8,000,000,000 and 10,000,000,000.

Two of the six patients treated were cured and discharged. In another, partial success was obtained, for while the fundamental schizophrenic symptoms were not altogether suppressed the hallucinations completely disappeared and the patient could be returned to his family. In the other three cases, the results were entirely negative. The authors emphasize the fact that the number of remissions exceeded that obtained with ordinary treatment, and express the opinion that since the supression of hallucinations is of such importance in the evolution of schizophrenia further work along these lines may justify the use of pyretotherapy in the treatment for schizophrenic hallucinosis.

NONIDEZ, New York.

PROPHYLAXIS AND THERAPY OF OCCUPATIONAL DISEASE. MICHAELIS, Fortschritte der Medizin **47**:605 (Aug. 9) 1929.

Many hygienic measures should be insisted on in industrial plants for prophylaxis against occupational disease. Illumination and ventilation in the work rooms, special rooms for eating, the use of rest periods, rooms for dressing and undressing, clean toilets and washrooms are indispensable. No employee should be permitted to eat without careful washing of hands and fingernails. Ventilation for the removal of poisonous gases or for dust and protection from dangerous machinery, especially for women and children, are usually made obligatory by law. Death from gas poisoning should not be acknowledged until rigidity develops, and artificial respiration should be undertaken for hours by the manual method. Pulmotors demand more people for operation but are superior to the manual method. In all factories medicaments and surgical equipment should be ready for any emergency, such as saline infusion, tracheotomy sets, gastric lavage, etc. The various antidotes for alkali, acid, aniline, arsenic, lead and other poisoning are reviewed in detail.

HART, Greenwich, Conn.

NERVE FIBERS AND NERVE CELLS IN THE "EPIPHYSIS CEREBRI." Giuseppina Pastori, Ztschr. f. d. ges. Neurol. u. Psychiat. **117**:202 (Nov.) 1928.

Pines determined that the pineal gland receives two nerve supplies: (1) central from the tenia thalami and ganglion habenulae with some fibers coming with the blood vessels from the tela chorioidea, and (2) sympathetic from the superior cervical ganglion. He was unable to find nerve cells in the gland. Pines says also that according to most recent investigations the posterior commissure supplies fibers to the pineal gland, particularly to the pineal stalk. Pastori was able to determine in animal material that the fibers coming from the posterior commissure and running in the tractus intercalaris are distributed to the pineal parenchyma. Pines was unable to determine any cells in the pineal gland which looked like nerve cells and stated that there are no such cells therein. In about 100 animals Pastori found only one typical ganglion cell which coincided with Hortega's description of heterotopic ganglion cells in the pineal.

ALPERS, Philadelphia.

THE DISTINCTION BETWEEN METABOLIC AND NERVOUS SYMPTOMS IN THYROID DISORDER. GEORGE M. GOODWIN, Am. J. M. Sc. **178**:83 (July) 1929.

The author divides the symptoms in cases of exophthalmic goiter into two groups, those due to disturbed metabolism and those due to disturbed nerve function. In the first group are included increased metabolic rate and weight loss; in the second, emotional instability, tremor, sweating, tachycardia and palpitation. A series of cases is presented to emphasize the distinction between symptoms resulting from disturbed metabolism and from a disturbed nervous mechanism. The latter is taken as evidence of altered autonomic function. Since nervous symptoms exactly similar to those of hyperthyroidism may occur without hyperthyroidism, the author believes that rarely should a diagnosis of hyperthyroidism be made unless there is a definite increase in metabolism. This is particularly true in the cases of nervous adolescent girls.

WAGGONER, Ann Arbor.

THE OCCURRENCE OF POSITIVE WASSERMANN REACTIONS IN THE SPINAL FLUID OF TUBERCULOUS AND OTHER NONSYPHILITIC CASES OF MENINGITIS. KARL SCHAFFLE and MAX RIESENBERG, Am. J. M. Sc. **178**:632 (Nov.) 1929.

The authors collected reports of eight cases which were definitely described as nonsyphilitic, and yet in each patient there was found on examination a positive Wassermann reaction in the spinal fluid. An inquiry was made as to the possibility of error in the technic employed. If the results could stand as facts, then some theories might be set forth: (1) with loss of brain substance there is an increase in lecithin and cholesterol in the spinal fluid to account for the positive Wassermann reaction, and (2) there was an abundance of micro-organisms in the spinal fluid causing the inflammation and giving rise to the reaction.

MICHAELS, Detroit.

INFLUENZA IN RELATION TO THE ONSET OF ACUTE PSYCHOSES. T. C. GRAVES. J. Neurol. & Psychopath. **9**:97 (Oct.) 1928.

The occurrence of influenza in persons without psychotic inheritance but with preexisting septic diseased states in the head may, by causing an exacerbation of the old process, precipitate serious mental disturbance. The constitutional symptoms of influenza need not be severe. The preexisting process may be responsible for pathologic changes elsewhere. Further toxemia may result from such changes. Subsidence of these secondary processes does not mean elimination of the original focus, and certain mental symptoms may persist after the acute attack or appear again after quiescence. The usual influenzal symptoms may vary greatly in these cases. The extent of a pathologic process in the skull may determine the degree of mental symptoms displayed.

FAVILL, Chicago.

THE CLINICAL INVESTIGATION OF THE AUTONOMIC NERVOUS SYSTEM IN FIFTY CASES OF SCHIZOPHRENIA. MURIEL L. M. NORTHCOTE, J. Ment. Sc. **75**:114 (Jan.) 1929.

Intravenous injections of 0.01 mg. of epinephrine and of 7.5 mg. of pilocarpine were given to fifty schizophrenic patients under uniform conditions. Observations were made of the blood pressure and pulse rate, Mannkopf's reaction, the oculocardiac and ciliospinal reflexes and some other features. From these observations the author concludes that there is nothing characteristic in the mode of reaction and that no definite correlation exists between the reactions and the clinical types of the disorder following the administration of these drugs. He also concludes that no reliance can be placed on the reflexes used as tests of the activity of the autonomic nervous system.

SINGER, Chicago.

THE CEREBRAL CIRCULATION: VIII. A QUANTITATIVE STUDY OF THE CAPILLARIES IN THE HIPPOCAMPUS. STANLEY COBB, Arch. Surg. **18**:1200 (April) 1929.

Cobb states that while much attention has been paid to the cyto-architecture and the myelo-architecture of the cortex, few studies have been made of the vaso-architecture. His present study aims to contribute to the knowledge of the cerebral circulation by giving quantitative data concerning the capillary blood supply of certain laminae of the rhinencephalon of the rabbit. The technic of the method used is described. It seems that Ammon's horn is somewhat less vascular than the motor cortex of the cerebral hemisphere. Furthermore, the brain as a whole has a much smaller capillary bed per unit volume than other areas such as muscle tissue.

GRANT, Philadelphia.

DEMENTIA PRAECOX AS A PHYSICAL DISEASE. C. B. BAMFORD, J. Ment. Sc. **75**:120 (Jan.) 1929.

This article contains a brief report of eight cases of "acute dementia praecox," with a clinical duration of "a few months." The principal features were confusion or excitement with rapid and profound physical wasting which was not checked by any remedies used. Autopsies were secured in six cases and the macroscopic appearances are briefly summarized. A report on the microscopic observations is promised as a later report. The author regards the macroscopic appearances as characteristic and indicative of physical disease; they include: (1) macrocephaly, (2) fibrosis of all bodily organs and (3) cardiovascular infantilism.

SINGER, Chicago.

PERIPHERAL INTERFERENCE IN KOJEWNIKOFF'S FORM OF EPILEPSY. J. L. Talmud, Ztschr. f. d. ges. Neurol. u. Psychiat. **117**:460 (Nov.) 1928.

Talmud reports a case of epilepsia partialis continua in the right hand of a patient, aged 40. The attacks occurred once or twice a month, lasted from three to five days, and were confined chiefly to the first and second fingers. It was found that the injection of procaine hydrochloride into the right median nerve caused the attacks to cease. Subsequently alcohol was injected into the nerve, followed by practically complete cessation of attacks.

ALPERS, Philadelphia.

A STUDY OF EQUILIBRIUM IN THE SMOOTH DOGFISH (GALEUS CANIS MITCHILL) AFTER REMOVAL OF DIFFERENT PARTS OF THE BRAIN. ATTILIO RIZZOLO, Biol. Bull. **57**:245 (Oct.) 1929.

The authors have studied equilibrium after removal of: (1) the end-brain; (2) the optic lobes; (3) the cerebellum; (4) the end-brain, optic lobes and cerebellum. They find that in the smooth dogfish, *Galeus canis*, removal of the end-brain, the optic lobes or the cerebellum does not effect disturbances of equilibrium. Equilibrium remains normal even after these three parts of the brain have been removed in the same animal.

COBB, Boston.

A CRITICAL REVIEW OF THE CEREBROSPINAL FLUID SUGAR. J. F. D. SHREWSBURY and G. F. WILLIAMSON, J. Neurol. & Psychopath. **9**:11 (July) 1928.

One hundred and fifty-one estimations of the sugar in the cerebrospinal fluid were performed by the Folin-Wu method on patients with various diseases of the central nervous system and also on persons showing no evidence of nervous disease. The previous observation, that a constant reduction, possessing diagnostic value, is present in tuberculosis and acute purulent meningitis, is confirmed. An increase was not found in epidemic encephalitis.

FAVILL, Chicago.

THE SEDIMENTATION VELOCITY OF ERYTHROCYTES IN THE PSYCHOSES. E. W. ANDERSON, J. Ment. Sc. **75**:80 (Jan.) 1929.

The author has studied seventy-three male patients suffering from various forms of mental disease, about one half of which were dementia praecox. He concludes from these observations that the sedimentation test has no value in the differentiation between various psychoses or in the estimation of the degree of improvement or of deterioration. From the tests in five cases of paresis he failed to find any striking acceleration of sedimentation in this disease. The sedimentation test is regarded as of value only as an aid in the early diagnosis of tuberculosis.

SINGER, Chicago.

DYSPHASIAS OF CORTICAL RIGIDITY AND THEIR TREATMENT: A PRELIMINARY REPORT. STEELE F. STEWART, Arch. Surg. **18**:1329 (April) 1929.

The three cases described represent three attempts to apply recently acquired observations concerning the sympathetic nervous system to the improvement of speech in patients with greatly increased muscle tone. They would seem to indicate that the muscles used in the formation of words and sounds are under the influence of the sympathetic nervous system to a certain degree, and that section of the sympathetic nerves in certain cases of dysphasia causes an improvement in speech. The cases are too few to be more than suggestive either of the exact difficulty that may be relieved or of the degree of improvement that may be anticipated.

GRANT, Philadelphia.

RELATIVE SENSITIVITY TO LIGHT OF DIFFERENT PARTS OF THE COMPOUND EYE IN ERISTALIS TENAX. WILLIAM L. DOLLEY, JR., and J. L. WIERDA, J. Exper. Zool. **53**:129 (May 5) 1929.

The method used for measuring the sensitivity of the ommatidia in different parts of the insect eye is described in detail. It was found that the ommatidia located at about the center of the compound eye of *Eristalis tenax* are more than fifty-five times as sensitive to light as those near the anterior end of the eye. Those at the posterior end are probably much more sensitive. Difference in degree of light adaptation is one of the main factors involved in the variability in the reactions of various specimens under identical conditions.

WYMAN, Boston.

THE SYNDROME OF HYDRODIPSOMANIA. I. CUNHA-LOPE, Encéphale **24**:441 (May) 1929.

Three young adults, one male and two females, all epileptic patients, gave histories of periodic attacks of uncontrollable thirst. All were characterized by an impulsive polydipsia, determined by a morbid visceral sensation. The attacks were of variable duration and probably should be considered as relatively rare equivalents of epilepsy. In all cases alcoholism could be definite ruled out. Associated with the polydipsia was a polyuria without glycosuria.

ANDERSON, Los Angeles.

THE SYMPTOMATOLOGY OF GLAUCOMA AND THE PROBLEM OF PATHOGENESIS. A. MAGITOT, Ann. d'ocul. **166**:356 (May) 1929; 439 (June) 1929; 565 (July) 1929; 610 (Aug.) 1929.

A series of four articles dealing with the symptomatology and pathogenesis of glaucoma stresses the importance of the study of the physical condition of the patient and general medical treatment in addition to the use of surgical measures. Although Magitot believes in surgery when indicated, he contends that best results in chronic glaucoma are obtained when the patient is treated for disease of the blood vessels.

BERENS, New York.

THE EFFECT OF CAFFEINE AND THEINE UPON THE EXCITABILITY OF THE SPINAL CORD. ATTILIO RIZZOLO, Biol Bull. **56**:379 (June) 1929.

The first application of caffeine or theine on the optimum motor point located on the ventral side of the spinal cord of the dogfish diminished the original chronaxia from 33 to 67 per cent; the fourth application increased the original chronaxia from 50 to 100 per cent. The sixth application effected an increase of as much as 200 per cent.

COBB, Boston.

SOME TENTATIVE CONCLUSIONS ON THE BOLTZ TEST IN GENERAL PARALYSIS OF THE INSANE. J. ERNEST NICOLE, J. Neurol. & Psychopath. **9**:26 (July) 1928.

Boltz's acetic anhydride test, when positive, was found to be almost invariably an indicator of paresis. A negative test is not a reliable indicator of the absence of this condition. The best results do not always agree with those of the globulin test; they tend to change after malarial treatment, but less frequently and rapidly than the globulin.

FAVILL, Chicago.

A METHOD OF DIFFERENTIAL STAINING OF THE HUMAN BRAIN. P. A. STEGALL, Anat. Rec. **42**:399 (May) 1929.

This article contains a description of a new method for staining whole brain sections made by the author's parowax method. The white matter is stained with an oil-soluble dye (methylene blue [methylthionine chloride, U. S. P.]) dissolved in cedarwood oil. The gray matter is stained with a water-soluble dye (mercurochrome-220 soluble).

COBB, Boston.

Society Transactions

GERMAN NEUROLOGICAL SOCIETY

Continuation of Report of Eighteenth Annual Congress, Sept. 13-15, 1928 *

DEUTSCHE ZEITSCHRIFT FUR NERVENHEILKUNDE **106**:213 (Dec.) 1928

DR. W. J. BERNIS, ROCHESTER, N. Y., *Abstractor*

PHYSIOLOGY OF THE VEGETATIVE CENTERS. J. P. KARPLUS, Vienna.

The first definite report that the spinal cord of vertebrates contains vegetative centers came from Friederich Goltz in 1863. Together with Freusberg, he studied the function of the lumbar cord of the dog. They found that there are centers present in the lower part of the cord for the genital organs, the bladder, the sphincter ani and for the large intestine, as well as for the blood vessels of the lower extremities and the pelvic organs. Since a center for the sexual impulse is also present in the brain, the authors were unable to decide whether the connection between the brain center and the reflex mechanism center in the cord is brought about merely through tracts or through interrupted ganglia. With the finger in the sphincter ani, one could bring on rhythmic contraction and inhibition of the same. Similarly, the rhythmic movement of the heart is brought about by the continuous bathing of the cardiac ganglia in the tissue fluids. The vascular centers of the lower cord are important to the tonus of the blood vessels of the lower extremities, uterus, bladder and the large intestine; yet after destroying the brain and the spinal cord, the tonus of the blood vessels does not disappear completely. Luchsinger showed the presence of sweat gland centers for the lower extremities in the cat in the dorsal and lumbar cord. It was known that nerve centers could be stimulated through nerve stimuli as well as by means of altered blood mixture, and that spinal sweat centers could be stimulated by raising the body temperature of the animal, by choking and by nicotine poisoning, and in many cases it could be brought on reflexly.

From extensive experiments, Vulpian concluded that the medulla is not the only point of origin for vasomotor nerves and their tonus. He assumed that the cord transmitted vasoconstrictor and vasodilator reflexes; and the different vasomotor nerves have their origin and their reflex centers in the entire extension of the gray matter of the medulla and cord. Stricker has shown that the vascular centers are arranged in interrupted positions; that the cervical cord contains vascular nerves, but not vascular nerve centers, which are present in the dorsal cord. It is known that the vegetative fibers do not come from all segments of the brain stem and the cord. It is reasonable to assume that their place of origin is to be looked for in those segments in which they leave the central nervous system: namely, in the brain, the area of the oculomotor, fascialis, glossopharyngeus and vagus nerves, then in the entire dorsal upper lumbar and sacral cord.

Experiments carried on by Goltz and Ewald, in 1896, have shown that a dog left only with the cervical cord may remain alive indefinitely, and that careful treatment of these animals will prevent trophic disturbances, inflammations and swelling. The tonus in the cordless animals returns after a short period of slight disturbance; the intestines function, the urine can be voided regularly, and delivery and lactation go on normally. In the author's opinion, the temporary paralysis of the organs after cutting or removing the cord depends on shock, and the most

* The other papers read before the German Neurological Society were abstracted by Dr. Bernis and appeared in the Archives, August, 1929, page 397, and September, 1929, page 600.

important life processes are decentralized. Naturally, the cord is important for the regulation of the vegetative processes, yet each individual part takes care of itself.

Two bladder centers are now assumed, one for closing the bladder, localized in the upper lumbar, and one for emptying the bladder in the lower sacral cord. Different centers are also assumed for ejaculation and erection, the exact localization of which is as yet unknown. André Thomas localized the pilomotor centers in man at the level of the first dorsal up to the second lumbar segment. Others assume also that pilomotor centers exist in the sacral cord. It is very likely that all vegetative centers have their segmental centers in the brain stem and the cord.

One distinguishes stimulatory and inhibitory centers, such as vasoconstrictor and vasodilator centers. The existence of such inhibitory centers has been definitely established. It is not certain, however, whether all stimulatory centers have also counterpart inhibitory centers. According to Bayliss, the vasodilators in the posterior roots are not to be considered as spinal efferent fibers but are identical with the sensory fibers, and reflex vasodilatation is an antidromic process. After extirpation of the abdominal gangliated cord and stimulating the vagus centrally, he found vascular dilatation of the lower extremities. He thus assumed also here that the stimulation is an antidromic reflex. Such an assumption presupposes the passing of the synapse in the central nervous system in the opposite direction, namely, the passing of an impulse from a cell body back to the axis cylinder of another neuron. To avoid this, Spiegel assumes, in addition to the vasodilator fibers in the posterior roots, which according to Bayliss have their trophic center in the spinal ganglia, in mammals also trophic centers in the gray substance of the spinal cord. Cardio-inhibitory, especially vasodilator, centers are known to be present in the cranial and sacral part of the parasympathetic system. Inhibitory centers for pilomotor and gland secretion have not definitely been established.

Porter has shown that the vascular reflex is increased by curare and is inhibited by alcohol without change in the tonus. He concluded that the vasomotor and the vasoreflex have different mechanisms, a conclusion which does not appear to be absolute.

More recently, Langley has shown that in the spinal cat, stimulating the central part of any nerve of the trunk or the sciatic produces a slight increase in the general blood pressure, while injection of strychnine produces a considerable increase. He calls attention to the important fact that after stimulation of a nerve in these cats there develops a mild grade of local reflex which is not definitely circumscribed. In spinal cats, Langley could find no effect on the pilomotor mechanism or on the sweat glands. This did not lead him to conclude an absence of spinal sweat and pilomotor centers. As for the blood pressure, Langley is of the opinion that the spinal vascular reflex is normally not of great importance, but becomes so under pathologic conditions such as after an injection of strychnine.

Discussing this problem, Karplus remarked that our organs undoubtedly possess a reserved force which ordinarily lies dormant and appears only under pathologic conditions which bring about an increase in the physiologic stimuli for the respective organ or tissue. This cannot be said with reference to the activity of the segmental vegetative centers, which under normal conditions, have rather an important function. The influence they exercise on the organs they innervate comes from three groups of stimuli. They are influenced by the alternating composition of the blood and the tissue fluid, then by the different afferent stimuli transmitted to them from the periphery, and again by the constant regulating influence which the higher vegetative centers exercise over them. Experimental physiology, which has brought excellent results, has often made the mistake of drawing hasty conclusions as regards normal activity. When the segmental is cut off from the higher vegetative centers it can no longer give a picture of normal function.

The higher vegetative centers exert their function mainly through the segmental centers. The somatic sensory and motor elements are individually represented in the corresponding spinal cord segments; higher up they are only indirectly so, and are rather in innervation groups, in extensive synergies. In the vegetative

system it appears that the individual vegetative elements are not quite so individually represented in the segmental centers in the cord and brain stem. For this, speak the interpolation of the peripheral ganglia and the fact that the postganglionic fibers are much larger in number than the preganglionic. Recently, Stöhr asserted that morphologically it cannot be proved that this nerve fiber is interrupted in a ganglion. The fact casts doubt on Langley's accepted two-neuron theory. At any rate, it may be assumed that the segmental centers have a far more reaching effect on individual directed innervation than do the higher vegetative centers. The segmental centers are only sympathetic, especially parasympathetic; that is, from them alone come sympathetic, and especially parasympathetic, impulses. From the higher centers come general directive impulses which are first elaborated on individually, in the segmental centers.

Considerable progress in this work has been made within the last few decades. The largest number of investigations were made on the midbrain. These may be divided into two groups: one, which was more concerned with its effect on the smooth musculature and glands, and the second which had for its object the study of the complicated process in the organs in which the vegetative innervations play the important part.

Karplus refers to the work which he and Kreidl have carried on in this field over a number of years. They employed faradic stimulation to the base of the midbrain; its effects were irritation phenomena of the ocular sympathetic, vasomotor effects, general increase of blood pressure, contractions of the bladder, sweating and secretion of tears, saliva and mucous membrane glands. The investigations were made on cats, dogs and monkeys. It was observed that by employing stimuli of sufficient strength that when the electrodes are placed posteriorly to the tractus opticus at the base of the midbrain they are capable of producing maximal stimuli in the cervical sympathetic, they were without effect on stimulating the dura, the hemispheres, the pes pedunculi or the infundibulum, while direct stimulation with the same strength of current of the trigeminus stem, in addition to expressions of pain, produced only a mild dilatation of the pupil. It was shown that stimulation from the frontal lobe to the cervical sympathetic passes over the hypothalamus, that on the other hand the hypothalamus exerts its activity on the vegetative organs entirely independently of the cortex. This gave the first proof that the hypothalamus is concerned with centers and not with tracts. It was found that one can succeed with minimal stimuli when the electrodes are placed not merely over the base of the brain but sunk in from 1 to 2 mm. deep in the brain substance. The authors accepted this as proof that the hypothalamus is interpolated as a central mechanism for vegetative functions, without at the same time assuming it to be the only one or that it alone is the only center for the cervical sympathetic. The authors also found that the subcortical vegetative centers are not limited to the hypothalamus or especially to the midbrain, but that they also include the area toward the lenticular nucleus.

The influence of the vegetative hypothalamus centering on the cervical sympathetic is bilateral. With very weak currents there was noticed, more in the monkey than in the cat or dog, a preponderance of the effect on the contralateral side of the cervical sympathetic. Stimulation of the hypothalamus develops, in addition to an excitability of the ocular sympathetic, also an inhibition of the sphincter branches of the oculomotor. By means of a combination of experiments, cutting through the cervical sympathetic and intracranial section of the oculomotor, it was possible to isolate the effect of the two nerves on the eye and thus obtain a clear picture of the alternating importance of the stimulatory and the inhibitory nerves for pupillary dilatation. The old conception that the oculomotor alone supplies the regulation of the movement of the iris was completely disproved. After intracranial section of the oculomotor and on long tetanization of the peripheral stump of the oculomotor, or on stimulation of the cortex or the hypothalamus, the authors were able to bring on dilatation of the pupil in the cat as well as in the monkey.

Similar experiments showed the importance of the hypothalamus centers as reflex centers. Here, there occurs essentially the switching over of pain stimuli to centrifugal impulses. In the sense of being a part of the pain transmitting mechanism, these vegetative centers may be considered as pain centers.

The effect on sweat secretion was definite, but not in all cases. Stimulating the cord in cats of from ½ to 1 year old will always produce sweat secretion, but not in younger or older animals. The effect on the general blood pressure was absent in a large number of experiments, although the other vegetative effects of the hypothalamus were present. The effect on the blood pressure has no relation to the pituitary or epinephrine content. Hypothalamus stimulation may bring on an increase in blood pressure after extirpation of the hypophysis and the adrenals.

The authors repeatedly observed that the hypothalamus is sensitive to pain, which was also observed in the monkey when this part was stimulated. But the other vegetative effects on stimulation of the hypothalamus should in no way be interpreted as being the result of pain reaction, for the effect was also observed in cases in which the pain reaction was excluded, such as in cases of mild or deep narcosis or when the brain was mutilated. The effect of cervical sympathetic stimulation remains unchanged after removing the cerebrum and the entire corpus striatum. When, however, the cerebral peduncle on the stimulated side is cut, without producing any other injury, stimulation remains without effect.

Observations on the tracts coming from the vegetative hypothalamic centers have shown that, in the cat, each half of the cervical cord transmits impulses from the brain stem to both cervical sympathetics. A crossing of the transmission from right to left does not take place in the cervical cord; this takes place only after passing this area of the cord. According to the experiences of the authors, the vasomotor and sweat impulses for the trunk and extremities in the cat and monkey (and with good reasons also in man) run mainly, but not exclusively, on the homolateral side.

Schrottenbach substantiated Karplus and Kreidl's observations that the hypothalamus contains sympathetic centers. He succeeded in producing isolated lesions in the regio subthalamica of the rabbit without injuring any adjacent part; manifestations obtained on the homolateral cervical sympathetic on frontal pole stimulation are lost after destroying the homolateral hypothalamus. As a permanent result of this, there remains a homolateral sympathetic paralysis of the eye (contraction of the pupil, narrowing of the eye and enophthalmus). Schrottenbach further observed, on destroying the hypothalamus on one side, that there developed breathing and vasomotor disturbances; the breathing becomes delayed and deeper, and the breathing reaction which normally follows on stimulation is greatly diminished or entirely lost; the loss of vasomotility is the same on both sides of the body. This author therefore concludes that, in the intact brain, the hypothalamus is the mechanism which innervates the breathing act and the blood vessels.

Leschke observed that injection of tetrahydronaphthylamine produces an extraordinary contraction of all the peripheral blood vessels, as well as an enormous rise in the temperature, but on cutting through the midbrain this effect cannot be obtained. Dresel comes to the following conclusions: 1. In the subthalamus there are vegetative centers which influence the blood pressure. 2. These centers regulate the blood pressure in such manner that in hypertension a reduction is brought about by stimulation of the parasympathetic and inhibition of the sympathetic; in low blood pressure an increase is brought about by stimulation of the sympathetic and inhibition of the parasympathetic. This keeps the blood pressure on a constant level. 3. A third vegetative center, important for the blood pressure, is found in the striatum and apparently in the paleostriatum. 4. This center is responsible for the height of the blood pressure in that it regulates the subthalamic center. By an increase due to stimulation of the paleostriatum, the midbrain reacts toward lowering the blood pressure. 5. It appears that the neostriatum has an inhibitory influence over the paleostriatal blood pressure centers. Karplus cannot unreservedly subscribe to the foregoing statements.

Lichtenstern substantiated Karplus and Kreidl's observations that stimulation of the hypothalamus will bring about contraction and emptying of the bladder.

Mammals and birds maintain unchanged their inner temperature against considerable fluctuation of the outer temperature. The heat formation may be influenced by changes in body oxidation and heat expenditure by surface circulation, ventilation of the lung and the formation of sweat. These processes are largely under the influence of the vegetative nervous system. Long ago, it was found that a disturbance of the heat regulation could be brought on by various injuries to the central nervous system; especially to be mentioned is the striatal puncture by Aransohn and Sachs. Some investigators expressed themselves against a too definitely circumscribed localization, as there apparently are many areas that control the heat regulation. Tigerstedt and Luciani deny the existence of special centers for heat regulation. According to Luciani, heat regulation is a function of the entire nervous system. Barbour, in 1912, showed that a portion of the corpus striatum may be influenced by heat and cold in an adverse manner and independently of the blood temperature, so that the application of heat acted as antipyretic and the application of cold brought a rise in the temperature. Jacoby and Römer, in 1912, after a series of experiments, came to the conclusion that heat regulation must be assigned to scattered ganglia in the cerebrum. In the same year, Isenschmid and Krehl were able to show that, in the rabbit, the tuber cinereum is indispensable for heat regulation.

Evidently the cerebral cortex exerts some influence over heat regulation through its control over skeletal musculature, as well as over the vasomotor and sweat secretions. This does not imply the assumption of the presence of heat regulation centers in the cortex. On the other hand, such centers are most likely present in the striatum and especially in the hypothalamus. In the hypothalamus, the nuclei tuberis were considered to be the seat of the heat regulation because these cell groups are well developed in mammals and birds. Nothing definite can be said as regards the relation between the striatum and hypothalamus as heat regulation centers. H. H. Meyer assumes a heat regulating center in the brain of a sympathetic nature in opposition to a parasympathetic cooling center. The assumption of a heat and cooling center expresses well a contrast regulation, and is in harmony with the knowledge of the service of the higher vegetative centers for the individual vegetative functions. Here, too, one must assume on the one hand a stimulating process, which at the same time promotes sympathetic and inhibits parasympathetic, and on the other hand a stimulating process, which at the same time promotes parasympathetic and inhibits sympathetic.

Aside from heat regulation, the higher vegetative centers undoubtedly take part in the different metabolic processes. Greater unity exists on their influence over sugar metabolism and urinary output. Claude Bernard's observation that a circumscribed lesion in the base of the fourth ventricle brings about an increase of sugar in the urine and polyuria has, with slight modifications, been substantiated, without the knowledge whether the lesion concerned tracts or a center. More recently, Brugsch, Dresel and Lewy reported experiments on metabolism and believe that they have established the presence of a sugar center in the medulla. Lewy, who conducted the anatomic investigations, believes that he has found, scattered within the dorsal vagus nucleus, the origin cells of sympathetic fibers which innervate the suprarenals. The nucleus periventricularis, a group of cells in the midbrain, Lewy considers as a superordinated center of the sympathetic vagus nucleus. The dorsal vagus nucleus he designates as a vegetative oblongata nucleus, because it shows the presence of sympathetic and parasympathetic cells. Brugsch, Dresel and Lewy came to the conclusion that in the posterior part of the vegetative oblongata nucleus lie sympathetic cells for starting the activity of the suprarenals and thus for sugar mobilization, while in the anterior part are vagus cells for the pancreas, therefore an increased glycogen formation. They also came to the conclusion that in the striatum there are present superordinated centers over the subthalamic centers, which are responsible for the height of the blood sugar.

Lewy also assumes that in his vegetative oblongata nucleus there are present sympathetic fibers not only for the suprarenals but also for all the important vital organs. Here, in a very small space, lie close together the cells for breathing, for the heart beat, nutrition and metabolism. This system has its caudal central representation in the vegetative oblongata and its most oral representation in the striatum. Karplus thinks that these observations need further investigation.

The appearance of polyuria after injury to the oblongata, as well as the importance of the midbrain for the regulation of water, has been confirmed by many investigators. The relation of lesions of the midbrain to changes in fat metabolism (Erdheim) and to genital atrophy (Aschner) has been firmly established. The influence of the brain on the entire metabolism, as well as on the albumin, purin and salt metabolism, requires further elucidation. Likewise, the part played by other parts of the brain in metabolism is not known. That the striatum plays a part in metabolism is very likely, but so far the proof has not been satisfactorily demonstrated. One thing hindering a clearer insight is the meager knowledge of the process in the peripheral organs during the different complicated metabolic processes.

The question is naturally raised: Can a localization be made of function in the higher centers, as, for example, in the midbrain? It can no longer be doubted that the midbrain stands in a more or less close relation to the entire vegetative life, and since psychic activities are accompanied by vegetative changes, the importance of the midbrain is thus not to be underestimated. New centers are being found. In addition to the aforementioned centers in the midbrain, a center for the sexual function is assumed. Here, too, is localized emotion and instinct, as indeed the tendency is now to assign to the midbrain a far greater influence over the psychic life than was the case formerly. Great care is necessary in assigning exact localizations. It is definitely established that a certain basal region in the midbrain exerts an influence on the activity of the cervical sympathetic, but that is not the case with the tuber cinereum. On the other hand, heat regulation appears to be connected only with the tuber cinereum. At present nothing definite can be said as regards the relation of certain cell groups to definite functions.

There is a close relation between the vegetative centers and the glands of internal secretion. It was pointed out before that an alternating composition of the blood acts on the excitability of the centers, and the internal secretion glands exert an influence on the chemical composition of the blood. The effect of the vegetative hypothalamic centers on increase of the blood pressure is independent of epinephrine and pituitary activity. Symptoms formerly assigned to the hypophysis are now attributed to the adjacent midbrain. The influence of the internal secretion glands on general metabolism is undoubtedly of considerable importance.

The vegetative centers undoubtedly are of importance for the trophic state of the vegetatively innervated organs, but it is not known how this influence is exerted. It is a question whether the trophic influence of the nervous system comes exclusively from the direct and indirect hormonal effect on the tissues, or there is, in addition, an exclusive trophic influence. This still remains an open question.

The influence of the central nervous system on the tonus of the body has long been established. The vegetative centers exert an influence on the tonus of the vegetatively innervated organs. Spiegel expressed himself against the conception that the skeletal musculature is supplied by the vegetative nervous system.

The alternating excitability condition of the vegetative centers is of the greatest biologic importance. It can be assumed that with this change are associated quantitative changes of the stimulus currents that run to the periphery. Karplus cannot accept the assumption of a biotonus based on the architectonics of the central nervous system. A direct connection between the individual sensory elements and the individual vegetative elements is unacceptable, and also unnecessary for effectiveness. The sensory elements also are not individually connected with the motor, yet by stimulating the different sensory elements with a stimulus of definite strength it is possible to produce general motor effects. When, through a reflection

or through a mental impression a change is brought about in the excitability condition of the spinal centers toward a certain frame of mind ("Stimmung"), one cannot escape the assumption that the reflection or the mental impression is first of all, a cerebral mechanism, and from here the spinal centers are stimulated. Such transmission of stimuli we must assume to take place over the transmission tracts.

Sleep and wakefulness are considered to be related to the vegetative nervous system. Such regulative mechanisms have been assumed to be present in the brain stem. The phenomenon of sleep is also assumed in the changeable effects between the vegetative nervous system and the cortex. Mauthner (1890) came to the conclusion that sleep is essentially an interruption of stimulation to the cortex, and the central gray matter is the location where interruption takes place. He pointed to the difference between hypnotics and narcotics; the former inhibit the function of the central gray matter, while the latter, on the other hand, stop the function of the cortex. Vogt (1895) assigned to this sleep center an active part — that a subcortical sleep center is the "regulating" point of sleep. Trömer (1912), on theoretical grounds, assigned it a place in the thalamus. Economo assumes a sleep center in the transition area between the interbrain and midbrain. With Pavlov's investigations on the conditioned reflex in mind, it appears to Economo as very likely that during the process of going to sleep inhibitions from this center go to the cerebrum and in this way bring about unconsciousness; an inhibition of the interbrain which leads to an inhibition of the stimulus transmissions may influence the body sleep, owing to the fact that a large number of the sympathetic, parasympathetic and vegetative centers, according to more recent investigations, are localized very close to the base of the adjacent interbrain. In his most recent work, Economo considers the sleep regulating mechanism essentially as a vegetative apparatus. He is of the opinion that the normal periodic changes between wakefulness and sleep are a vegetative function of the entire organism, which for its regulation, like other vegetative functions, has a representation in the central nervous system; that in the transitional area between the interbrain and the midbrain is the sleep regulating center which is active during sleep and waking periods.

It is undoubtedly possible in the decerebrated animal to make out a state alternating between that which more nearly resembles wakefulness and one which more nearly resembles sleep. Somnolence was observed in man (Orzechowsky) after an inflation in the third and lateral ventricles. Demole was able to bring on somnolence and sleep by injecting minimal doses of calcium chloride into the infundibulum. Mehes, on the basis of pharmacologic investigations, comes to the conclusion that the part of the hypothalamus near the aqueduct is the most important area for sleep. In contrast to this, Spiegel and Inaba, from experiments on dogs, reached the conclusion that the thalamus, not the neighborhood of the aqueduct, is the area for the regulation of sleep. Lhermitte and Tournay believe that the sum of clinical, anatomic and experimental experience indicates that the basal region of the third ventricle is an area which when diseased will bring on sleep. They assume a mesencephalo-diencephalic regulation apparatus. Hess was able to produce somnolence in cats by injecting ergotamine (1 mg. in a few drops of fluid) into the third or the lateral ventricles. This led him to develop a theory concerning the alternating effects between vegetative and psychic functions.

Knowledge is limited as regards the relation of the cortex to the vegetative system. Clinical and experimental experiences make it certain that different vegetative functions may be influenced by definite cortical areas; as to how this is brought about there is no unanimity. There are not sufficient grounds for the assumption of the presence of regulating mechanisms in the cortex. With greater justice it may be thought that the subcortical regulating mechanism receives from the cortex a kind of check or curbing. On the other hand, there is no doubt that our entire animal life, especially the activity of the brain cortex, is under a vegetative influence.

PHARMACOLOGY OF THE VEGETATIVE NERVOUS SYSTEMS. E. P. PICK, Vienna.

The degree of susceptibility possessed by particular parts of the body for certain toxins depends on many conditions. It depends on the concentration, quantity, penetration and duration of action of the drug, the tonic state of the affected area produced by the central organs, and on the existing state of irritability conditioned by the fluid mixture, in which the acidity or alkalinity and the increase or diminution of promoting or inhibitory salts and hormones play an important part. These observations lead to a classification of drugs into sympathicotropic, vagotropic and in many cases amphotropic types of activity, which may be recognized by experiments on different organs and by clinical observations. Nearly all external influences — light, air, external temperature, intake and quality of food, hunger and thirst, rest and work, and the most subtle changes in the physical, chemical and hormonal composition of the blood and fluid as well as the existing psychic presentation — are capable of bringing about changes in the vegetative reactions and hence again of the psychic condition. In most therapeutic advances of modern times — irritant bodies, fever therapy, treatment with hormones and vitamins — the success obtained must be assigned largely to an alteration in the vegetative nervous systems. The necessary adaptation of the vegetative life to the external and inner world requires a constant change in tonus and irritability of all parts of the vegetative nervous systems and hence in the power of resistance against irritants of the most varied kind.

While pharmacologic investigations have afforded knowledge of the therapeutic influence of the peripheral nervous system, little is known of the pharmacologic influence on the nerve centers; which increase or inhibit the irritability of the vegetative nerves, regulate partial function, and maintain equilibrium between agonists and antagonists.

The irritability of the vegetative centers, lying mostly in the midbrain, is determined from regions at a higher level; they appear to be regulated by some of the hormonal glands among which may be considered the posterior lobe of the hypophysis, the supratuberal hypothalamus area and the tuber cinereum itself. From these parts of the brain, secretions are given off to the cerebral fluid from which may be isolated at least two chemical substances (Kamm and his co-workers) that strongly affect the blood pressure and the uterus. They control the state of irritability of the vegetative midbrain centers in such manner that their lack or the diminished activation of the part of the brain and its assumed center in the nucleus supra-opticus leads to marked functional disturbances of the water center in the thalamus (diabetes insipidus) and of heat regulation (marked lowering of the temperature) and apparently also disturbances of other centers of metabolism. An increase of these substances in the fluid is observed after excitement.

Excitation, particularly deinhibition as well as inhibition, can be brought on by centripetal nerve stimulation, above all through the blood which gives adequate stimuli for the enlistment of the vegetative centers. This can be observed from an adequate breathing stimulus, carbonic acid in the blood, and may be seen experimentally in the effects on the water, salt and sugar centers, with a rise and fall of the quantity of water, sodium chloride and sugar in the blood. An oversupply or a diminution of these substances in the blood stream and in the body tissues are the strongest stimuli for a central readjustment of all peripheral reacting organs in bringing about a normal equilibrium between the blood and the tissues. This can be observed in the heat centers of the striatum and thalamus; blood of subnormal temperature acts as a sympathetic heart stimulus and the blood in fever as a parasympathetic cooling stimulus. The rule can be laid down that only overstimulated or understimulated centers are sensitive to opposite stimuli and bring about the opposite regulation; it is not the normal, but a heat center overstimulated by fever that can be braced up by antipyretics. A mild third stimulus can affect an oversensitive water center and cause fluid from the tissues to be given off to the blood, while a normal or over hyposensitive water center can be affected by hypophysis secretion only after an increase of water in the blood.

It is possible that remedies may act centrally either as sedatives or as stimulants, the preconditioned effect depending on the state of the part affected. Experimentally, exact establishment of the susceptible area or points of the central nervous system by pharmacologic methods meets with greater difficulties than a similar study of the peripheral nerves, since the effect spreads to larger brain areas and hence embraces at the same time many nuclei. The changed content of sugar or salt in the blood also changes the susceptibility of the heat center; on the other hand, antipyretics are capable of inhibiting the salt center. Again it should be remembered that insulin will lower a high temperature; it may even counteract the effect of fever toxins such as B-tetrahydronaphthylamine, and may increase the readiness for spasm and stimulate the salt center in a manner similar to that of the thyroid hormone. A sharp limitation of the pharmacologic effect between the animal and interbrain centers is impossible since a large number of remedies influence both the vegetative and the animal centers. This will indicate the difficulties of pharmacologic experiments as regard its effect on local areas. Mindful of these limitations Pick still believes that the answer to certain pertinent pharmacologic experiments will be of service in the diagnosis and therapy of diseases of central origin, and therefore a discussion of the effects of sedatives and stimulants may be of importance to the physiology and pathology of the vegetative centers.

All true narcotics must be toxic to the cerebrum, since they quickly dull the pain centers in the cerebrum. The disappearance of cortical sensibility, as during ether or chloroform narcosis, takes place even before loss of consciousness, and before the unchanged irritability of the thalamic motor reflex mechanism. Some hypnotics must also make their primary attack on the cerebrum. This is especially true of the opiates, among which is morphine, which paralyzes the pain centers of the cerebrum before it brings on sleep. The quick disappearance of certain inhibitions, effected through the cerebrum, permits also the deduction that other hypnotics, which do not influence or only partially influence the sensation of pain, attack first the cerebrum; examples of this are alcohol, amylenehydrate and chloralose, which deinhibit the interbrain motor centers. Chloral hydrate, U. S. P., which raises the cortical inhibition to the vegetative brain stem centers, and paraldehyde, which similarly deinhibits the water center lying in the brain stem, are also examples. The bromides, on the basis of their specific effect in nervous irritability, must be considered as remedies affecting the cerebrum. Most of the cortical hypnotics are unable to inhibit the vegetative centers, the interbrain and the midbrain region, and in small doses are unable to control the motor excitability or coordination disturbances of the brain stem.

Fundamentally different is the action of the urea products, with which most modern hypnotics must be included — barbital, phenobarbital, somniphen, phenylethylhydantoin, chloretone and the valerian preparations. From the effect of these substances, it appears that their point of attack is not the cerebrum but rather the brain stem in the neighborhood of the vegetative centers. Many of them — barbital, especially phenobarbital, phenylethylhydantoin and chloretone — exert a sedative influence on the thalamic motor brain area when administered in doses insufficient to induce sleep. They influence favorably the most severe choreic disturbances of coordination; even in small doses they check the irritable vomiting center, diuresis center and perhaps also — as for example, barbital — the heat center; further, when given in the usual doses, their presence can be shown in the brain stem (corpus striatum and thalamus), but not in the hemispheres, cerebellum or medulla. A distinction is therefore made between cerebral and brain stem remedies.

Hypnotics Affecting the Cerebrum	Hypnotics Affecting the Brain Stem
Alcohol	Barbital
Amylenhydrate	Phenobarbital
Chloralose	Phenylethylhydantoin
Paraldehyde	Chloretone
Chloral hydrate	Valerian
Bromide salts	Magnesium salts
Morphine	

That sleep remedies are divisible into two types depending on their point of attack and their sleep-producing qualities, and that their effect is not to be assigned to the cerebrum alone but also to the brain stem, are further substantiated by a number of experiments. After removing the cerebrum and the corpus striatum, not only does a spontaneous change between wakefulness and sleep take place (Goltz, Rotmann, Karplus and Kreidl) but sleep can be brought on by different remedies. In such animals, sleep, even deep sleep, can be induced with much smaller doses than in normal animals. All sleep remedies, regardless of whether they are cerebral or brain stem hypnotics, in striatum or thalamus animals bring on sleep which begins with paralysis of body posture and of the labyrinthine reflexes, and with complete deinhibition of the thalamic pseudo-pain center. It should be noted that the more readily induced sleep in decerebrate animals can also be brought on with substances that otherwise affect first the cerebrum. This indicates that cortical hypnotics in their further action inhibit brain stem tracts and in this way bring on sleep. On the basis of this experience there is little justification for the contrary assumption that in the end all sleep remedies, directly or indirectly, block excitations in the brain stem and that there is no sleep remedy that does not affect the brain stem. In addition, experimental injuries to the thalamus, corpora quadrigemina and aqueduct (Mehes, Spiegel and Inaba) bring on a continuous sleep that often lasts for several days.

Some drugs that affect different parts of the brain in different ways, partly stimulant and partly inhibitory, give some insight into the part played by the cerebrum in bringing on sleep. While atropine will produce the strongest excitation in the cortex and brain stem, hyoscyamine, and above all scopolamine, is sedative in man and under certain conditions may produce sleep. The favorable effect of scopolamine in severe coordination disturbances in Parkinson's disease and in the motor overexcitability of mania indicates that the main effect of this drug is on the motor coordination center of the brain stem, inhibition of which undoubtedly passes over to the thalamus, the brain stem area for sleep mediation; on the other hand, bulbocapnine, which arrests the labyrinthine and postural reflexes, attacks the region above the optic thalamus and therefore does not induce sleep.

Effective as are scopolamine and atropine in man, these alkaloids exert little toxicity on plant-eating animals. It was suggested that the blood of these animals is capable of destroying the toxin. But it was found that even in these animals, if bromides or very small doses of morphine are first given or the brain is removed surgically, scopolamine can cause typical sleep.

Another fact of importance is that animals in which sleep was induced with magnesium salts by the Meltzer and Auer methods can be wakened almost instantaneously by intravenous injections of calcium chloride. The newer pharmacologic analyses of thalamic animals have shown that very small doses of magnesium chloride bring on sleep; that the awakening effect of the calcium salt depends on a stimulation of the cerebrum, or even more likely the corpus striatum, since decerebrate animals may still sometimes be wakened from sleep produced by magnesium salt by the injection of calcium salt; this is not true of the thalamic animal which may even be put to sleep by calcium salt. The calcium salt therefore produces opposite effects in two adjacent parts of the brain; it stimulates the striatum and acts as a sedative on the area of the thalamus. That sleep induced by magnesium can so readily be interrupted by calcium depends on the fact that the magnesium induces sleep in the thalamic brain stem, while the stimulatory effect of the calcium is set free in the striatum, thus producing a prompt awakening. Should the striatum be eliminated, as it is with most other sleep remedies, then an awakening with calcium chloride would be impossible. This leads Pick to conclude that the opposite stimulatory conditions of the cerebrum, striatum, and the approachable parts of the thalamus for sleep and waking effect have a mutually influenced boundary line; any alteration in the state of one influences the sleep and wakefulness of the other part.

The constant latent susceptibility for sleep of the thalamic region is therefore disturbed mainly by waking stimuli which come from the cortex or from the

striatum; therefore, every depression in the action of these parts and obstruction to the activity of the stimulatory tracts is a preliminary condition for the transition of sleep to the sleep-predisposed thalamus. According to this conception, only one of the regulating mechanisms for the setting in and the depth of sleep could be assigned to the cortex and perhaps also to the striatum. The nearer to the thalamic sleep centers the stimulatory tracts are blocked, the more prompt will be the setting in of sleep and the more sound the sleep will be. This explains why thalamus animals will be put to sleep by a number of drugs which have no effect on the normal animal; for the same reason such substances as ergotoxine, apomorphine and calcium salts, which are not hypnotics, are capable of bringing on sleep when the stimulatory influence of the forebrain over the thalamus has been removed, or when these substances in sufficient concentration have been brought directly to regions where the stimulant tracts to the thalamus can be checked.

On the other hand, all substances which increase the centrifugal stimuli of the cerebrum and the striatum or the centripetal stimuli from the periphery of the thalamus region must bring about a lack of sleep, or insomnia. Not only do caffeine, cocaine and camphor, which stimulate principally the cerebrum, interfere with sleep, but also subcortical stimulatory poisons — such as B-tetrahydronaphthylamin, epinephrine and ephedrine — act in the same way. Here, too, it should be noted that substances, such as caffeine and cocaine, which normally produce marked waking stimuli in the brain and readily break through chloral sleep, are entirely ineffective in decerebrate animals put to sleep with chloral hydrate, while substances which attack the vegetative brain stem centers, such as tetrahydronaphthylamin or ephedrine are capable of awakening even decerebrated animals from a deep chloral sleep. Cardiazol and exeton have a similar effect on decerebrate and thalamus animals.

All attempts at explaining the onset of sleep as due to something occurring only in the cortex meet only a part of the problem, and not the chief problem. For the same reason it appears that the view that Pavlov's "conditioned reflexes" are dependent on cortical function and thereby explain the process of sleep is not well founded. Everything points rather more to the older hypothesis of Mauthner and Trömmer and the modern views of Economo and Pötzl based on clinical and pathologic anatomic observations, that spontaneous sleep as well as sleep induced by medication depends on the irritability of the thalamic boundary area in the interbrain and midbrain.

The statement concerning the influence of hypnotics and narcotics on the sleep regulating center cannot be separated from the lessons derived from the postural reflexes. The effect of the drugs appears evident in cramp conditions, since some of them as cocaine and camphor, according to the investigations of Moritas on decerebrate animals, affect by preference the cerebral hemispheres. On the other hand, picrotoxin, strychnine and phenol affect more deeply lying centers; yet it must not be overlooked that in man and some animals, cocaine and camphor may also stimulate deeper lying centers. Camphor may also produce an increased reflex irritability in the isolated cord of the cat. The experience gained from thurjon, another form of camphor, shows that clonic and tonic cramps may be obtained even after the removal of both cerebral hemispheres. The well known psychic and motor morphine irritability of the cat depends only partly on irritation of the cerebrum; the greatest part of it depends on stimulation of the motor brain stem, since this effect can be obtained also in decerebrate cats.

It is unnecessary to point out that some of the cramp-producing toxins, in addition to their influence on the typical motor and indeed animal reflex centers, also influence vagus centers; others affect mainly sympathetic centers. Thus picrotoxin, a typical parasympathetic toxin, stimulates the vagus center in the medulla, the oculomotor center in the corpora quadrigenima, the parasympathetic, salivary and sweat centers, and like santonin, camphor, cardiazol, phenol, aconitine and veratrine reduces the temperature, apparently through the intervention of parasympathetic stimulation of a cooling center, perhaps as a result of central inhibition of heat production. Other poisons, such as caffeine, cocaine and

B-tetrahydronaphthylamin, have the character of central sympathetic stimulatory poisons, with central vasoconstriction, increase in the heart beat, central sympathetic pupillary dilatation and raising of temperature through stimulation of sympathetic heat centers in the hypothalamus as their signs.

Sherrington's pseudo-pain reflexes, coming from a center in the midbrain through sympathetic tracts, express themselves as defensive movements: crying reflexes, changes in breathing, tear secretion, distortion of mimicry, pupillary dilatation and other signs of displeasure and pain. Normally, these pseudo-affective reflexes are incited only through the cortical pain centers and are checked through special inhibitory tracts from the cortex. Most remedies that eliminate the sensation of pain from the cortical area prevent, at the same time, stimulation of the hypothalamic pseudo-pain center. Thus, they interrupt the reflex tract from the cerebrum to the midbrain.

Drugs which induce sleep and influence pain also act on fever. Most hypnotics and narcotics calm the irritated heat centers in the corpus striatum and hypothalamus. Experiments carried on by Aronsohn and Sachs and by Isenschmidt and Krehl show that thalamus animals are still capable of heat regulation, but when the midbrain is eliminated before the corpora quadrigemina or a separation of the tuber cinereum is made from the corpora mamillare all heat regulation stops; cutting through the cervical cord makes the animal poikilothermic; sectioning of the thoracic cord damages only physiologic heat regulation by increasing the elimination of heat. Therefore, regulation takes place mainly in the basal and middle posterior two-thirds, apparently in the central gray matter of the midbrain, and is controlled by a superordinated striatal center. Consequently, it is not surprising that antipyretics, the point of attack of which is certainly near the sleep-regulating center, can be substituted for by hypnotics or be considerably strengthened by them. On the other hand, the common effect of sleep and fever remedies, by eliminating irritation to the thalamus, must increase the soundness of sleep. The same holds true as regards the elimination of pain tracts. That antipyretics are also analgesic lies in the assumption that the heat and pain transmitting tracts and nuclei lie close together in the midbrain; therefore these remedies also exert a favorable influence on adjacent midbrain and interbrain centers of different function.

The central influence of cellular metabolic processes — water, salts, sugar, fat and albumin elimination — is not surprising; furthermore, the central regulation of the absorption and elimination of substances in the organ cells — muscles and other tissues — thereby bringing about a regulation of tissue turgor and tonus, is understandable. Alteration in the fluid changes of striated muscle, its permeability, as well as a number of other metabolic processes (ammonia, glycogen, lactic acid and lactacidogenic substances), was shown to take place after excluding the sympathetic tracts. It is especially to be observed that Glass, as a result of selective central toxic effect and operative injury to the striatum and thalamus, observed changes in the absorption and excretion of water in the striated muscle of the rabbit. Here also belong the inhibition of albumin decomposition through nuclei of the subthalamic heat regulating area and its deinhibition through operative or drug elimination. The investigations of L. Bogendorfer and G. Rosenow as well as of Heilig and Hoff indicate that even the blood picture is considerably influenced by brain stem centers.

Finally, it is to be noted that the reflex as well as the directly stimulated vomiting centers may be controlled. Here also, sedatives acting on the thalamus such as phenobarbital, barbital, valerian preparations and especially chloretone have proved successful, stopping even apomorphine vomiting.

Breathing and circulation of the blood possess important regulatory centers in the midbrain. This can be observed from the beneficial influence of morphine, chloral hydrate and other hypnotics in edema of the lungs. Libman and others have observed attacks of edema of the lungs before apoplectic insults and in pre-eclamptic women with otherwise no disease of the heart: Trömer observed edema in the postapoplectic paralyzed limbs; these observations probably depend on disturbances in these centers.

PATHOLOGY AND CLINIC OF THE VEGETATIVE NERVOUS SYSTEM. E. FRANK, Breslau.

The vegetative system is composed of the complex receptor apparatus of muscle and gland cells, of centers and tracts in each of the antagonistic nervous systems, and of the endocrine organs — the structures that elaborate chemical substances with physiologic activity in relation to the vegetative nervous system. Frank accordingly considers the problem of the somatic vegetative neurosis in relation to the structure and directing influence of the receptor apparatus, then considers the importance of the vegetative midbrain centers for pathology in close association with the fundamental question whether, aside from stimulation and inhibition of motility and secretion, the centers may not also exert an influence on the metabolism and the trophic state by means of a humoral intermediation.

The conception of the receptor apparatus that has developed from pharmacodynamic analysis, from an exact determination of the points of attack of drugs which have an action similar to electrically stimulated vegetative nerves and which therefore are designated as sympathicomimetic and parasympathicomimetic substances. These mimetic drugs are not only found in the alkaloids of plants but are also formed in the animal body and are passed into the blood; that is, they have characteristics of hormones. Of special interest are epinephrine, a sympathicomimetic (ephedrine, a plant derivative, being closely related to it), and choline, especially its acetylester, a parasympathicomimetic (muscarine, a plant derivative being closely related to it).

Formerly, it was assumed that toxins with peripheral properties, whether stimulatory or inhibitory, attacked the nerve-endings, which on the basis of structural differences were also distinguished physiologically from the nerve fibers. This conception was disproved thirty years ago by Lewandowski. He found that the dilatation of the pupil, by epinephrine, will take place even many weeks after removal of the superior cervical ganglion, that is, after degeneration of the postganglionic fibers has definitely been established; from this he concluded that there must be a muscular attack by the epinephrine. This conception, however, is too simple. According to Langley's investigations, these drugs apparently do not attack the contractile muscle itself or the secretory gland substance, for its functional effect can be blocked by means of specific inhibitory substances without interfering with the irritability of the muscle or gland. He therefore assumes that toxins with the so-called nerve-ending activity, generally exert a trophic influence over the corresponding organ, but do not affect its main activity, a stimulus receiving and stimulus conducting side chain of the protoplasm which he designates as a receptive substance. Boeke considered the periterminal network, which he discovered and which is found between the nerve-ending net and muscle plasma, as the morphologic basis of the receptive substance. But this identification is not justified, since after sectioning of the nerve, the periterminal network becomes equally degenerated, although somewhat later than the nerve-ending, and at a time in which the receptive substance is especially active the periterminal network has already completely disappeared.

It has been known for some time that the vagus inhibition of the heart caused by an accumulation of potassium salts in the blood can be counteracted by the addition of calcium salts. From accumulated investigations it can be said that a relative increase of calcium ions acts on the vegetatively supplied organs as do the sympathetic and epinephrine, and that a relative increase of potassium ions acts like the parasympathetic and acetylcholin.

It can therefore be said that each of the two groups produces opposite effects; the heart and blood vessels, on the one hand, and the smooth muscle of the hollow organs and canal system, on the other, are differently influenced. The vagus group inhibits the motility of the heart and stimulates the bronchial tree, gastrointestinal canal, bladder and uterus. But the attacking point of the ions cannot be identical with that of the nerves and with that of the endogenous pharmacons. Atropine, which inhibits the parasympathetic irritability and that of acetylcholine, has no influence on the effect of potassium. Likewise ergotamine, the effective

principle of ergot, which specifically blocks the sympathetic impulse and epinephrine activity, is without influence on the calcium activity. The ions therefore must attack peripherally further cellward than do the nerve and the hormones.

The receptive apparatus, or as Kraus and Zondek term it, the vegetative driving part of the cell, can best be understood as being composed of two fang arms or aerials coming from a common base. A distinction is made between an "epinephrinophil" fangarm (in contact with the sympathetic) and a "cholinophil" fangarm (in association with the parasympathetic); the first is set in activity by ergotamine, the latter by atropine or scopolamine, and the common base is considered as ion sensitive in such a way that potassium and calcium ions, by the absorption of both and combination with the colloid mass of the ground substance, constantly attempt to displace one another. Frank proposes to designate as "sympathetic, in a physiologic sense," the sum of all those nerves that become sensitive by an epinephrinophil aerial, and as parasympathetic the sum of all nerves which are sensitized by a cholinophil aerial. The ion sensitiveness of the receptor or the "vegetative impulse part of the cell" permits the assumption that it is in close relation with the marginal surface of the cell, or the so-called plasma membrane.

Conformable to Howell-Zondek's hypothesis, Frank embraces cation activity in the physiologic excitation process. He is inclined to assume that the sympathetic and epinephrine has greater effect than the calcium, and the parasympathetic and the acetylcholine than the potassium; for example, the impulse conducted through the cholinophil fangarm leads to a mobilization of fixed internal potassium, and thereby to a concentration of the potassium ions in the colloids of the marginal phase. In support of this can be mentioned, Howell's observations that under the influence of vagus stimulation there is an increase of about 20 per cent of potassium ions in the fluid of the mammalian heart.

As regards the receptor apparatus, it must be mentioned that when the contact with the nerve is cut, the fangarm will become hypersensitive and there will be a degeneration of the postganglionic fibers. The reaction observed is the same as if the nerve were being stimulated: "paradoxic" pupillary dilatation after removal of the superior cervical, pupillary contraction after removal of the ciliary ganglion, paralytic salivary secretion after removal of the chorda tympani. After sectioning a peripheral nerve which contains the vasoconstrictors, as a rule, reddening and hyperthermia are not found, but rather pallor, cyanosis, lowering of temperature and stagnation, apparently because the arterioles henceforth depend on humoral stimulation. Finally, it should be noted that undoubtedly there are also stimuli which attack the vegetative receptor apparatus at the point of junction with the conducting apparatus; then the effect is no longer that of stimulating one organ and inhibiting another, but shows everywhere a similar effect. The well known ional stimuli of this type are barium, with its universal contractile quality, and magnesium, as a relaxing influence. Of the internal secretions, it is to be noted that all smooth muscles are stimulated by pituitrin and thyroxin.

The second point for consideration is the central nervous influence of the vegetative systems. Most physiologists and pathologists consider that the gray substance which surrounds the ventral part of the third ventricle, the regio subthalamica, the tuber cinereum and its adjacent area, is the upper directing force of the vegetative system. They also believe that biologically it is most difficult to assign concrete functions to these generalized areas, and that most careful criticism is essential. Attempts have been made to establish certain principles from cytoarchitectonics and fiber architectonics, from experimental results and from collected clinical and anatomic cases. While such studies may have value, the number of established facts is still very limited. Especially is it premature to hold a definite opinion as regards the detailed functioning of the base of the midbrain.

When the question is raised as to which disease manifestations can be definitely localized in the hypothalamic area, only one fact appears certain. The development of fever, as well as physiologic heat regulation, is associated with the area on both sides of the midline of the tuber cinereum and its immediate neighborhood. When the "temperature center" which is assigned to this area is stimulated,

there results a complex of sympathetic phenomena: marked contraction of the skin arterioles stimulation of oxidation in the liver, with glycogen mobilization by way of the splanchnic and increase in heat production in striated muscle — the rigor of which is to be considered as an indicator of fever — through the sympathetic tract discovered by Boeke. In addition, there are auxiliary actions: contraction of the blood vessels supplied by the splanchnic, strengthening and increasing the activity of the heart to bring about an exchange of blood in the muscles, as well as a renewal through splanchnic intervention of stimulation of epinephrine secretion which is essential for sympathetic activity. The temperature center therefore embraces the activities of a number of coordinate sympathetic centers, bringing about a unification which, teleologically speaking, serves for the maintenance and formation of heat. Physiologically, the center is stimulated by cooling, touching, or when the inner body is threatened by overheating. The physiologic stimulus comes through impulses which are conducted from the temperature nerves of the skin, and through the slightest lowering of the blood temperature. The center is, furthermore, unusually sensitive to all mechanical lesions in its vicinity, especially to a large number of dissolved, colloidal or suspended impurities of the blood, particularly to foreign blood proteins.

The study of heat regulation and fever permits the assumption of certain general principles regarding the function and purpose of the vegetative central apparatus in the midbrain. It can be said that individual centers are not represented here as in the medulla, but that the performance in this place of the individual centers toward vegetative results is coordinate. It further appears that the nervous substance of the base of the midbrain is very sensitive to blood stimuli of physical and chemical nature, and that metabolism receives important direction.

The study of metabolism regulation by the vegetative midbrain centers has of late received considerable attention. According to Frank, it is not certain that the subthalamic area contains circumscribed centers for individual characteristic metabolic functions, such as for quantity of water, the exchange of sugars, the fat and its distribution. It is not possible to isolate such centers, and he believes that the position usually taken on this problem is not justified.

Next to heat regulation, the regulation of water output was assigned as a function of the midbrain. According to many investigators there is no doubt that puncture of the hypothalamus anteriorly or posteriorly near the base of the infundibular funnel will gradually develop an increased flow of urine, which will gradually subside. Even a superficial injury in this area will have a similar effect. Occasionally, the effect of the injury remains permanent. The polyuria caused by hypothalamic puncture remains even when the hypophysis is uninjured; it is also present when the hypophysis has been removed from two to three weeks before. The difficulties of interpreting the hypothalamic puncture, associated especially as it is in narrow space with an incretory organ, especially with one possessing chiefly a most powerful effect on diuresis, appears therefore to have been overcome by experimental art. When, in addition, it is considered that in nearly all cases of organically conditioned diabetes insipidus, a disease process can be found in the infundibular region, a water regulating center in the tuber-cinereum appears most probable. This center must be irritated by the puncture and not put out of function, since after sectioning the brain stem posterior to the midbrain or after cutting through the cervical cord an increase in the diuresis is not noticed. The difficulties for the assumption of a purely nervous regulation came from the observations of Bailey and Bremer that the effect of a hypothalamic puncture does not diminish in activity even after total removal of the kidney. These authors assumed that the urine flow does not come primarily from the kidney but depends on the water inflow from the tissues into the blood brought about by nerve mediation. This conception is no longer tenable. Helen Bourgnin has shown that cauterizing the tuber cinereum causes marked and undiminished polyuria, especially when the cord is cut through at a lower cervical or upper dorsal level, therefore after a procedure that at once stops heat regulation. How then can the center exert its influence when the long tracts which go to the

required organs are no longer functioning? Greving and Pines and Stengel have shown that a thick complex bundle of nerve fibers passes through the hypophysis pedicle into the posterior lobe of this organ; on the other hand, the powerful antidiuretic effect of the posterior lobe secretion is known; it regulates the disturbance of urinary output as insulin regulates sugar. If it is assumed that the center is not irritated by the puncture or the cauterization, but that it is paralyzed, it would permit the assumption that the impulses are absent for the removal of the increta necessary to maintain constant the body fluid. But the puncture is also effective after extirpation of the hypophysis; this explanation is therefore not valid. Finally, the hypothalamic puncture does not indicate the existence of a "water center." Frank is of the opinion that the lesion does not disturb a nervous but rather a humoral mechanism. It is known that the hypophysin does not pass directly into the blood, but passes through the tissue of the stalk up to the ventricle where it mixes with the liquor and in this way reaches the blood. A lesion of the tuber with inflammatory hemorrhagic products embedded in the tissue will temporarily, more seldom permanently, render it more difficult for the passing on of the hypophysial increta to the ventricle. The remarkable fact that for a long time after removal of the hypophysis a hypothalamus lesion is accompanied by polyuria has found a satisfactory explanation through the work of Trendelenburg and Sato. These authors showed first that the hypophysis substance, which is always present in the liquor, disappears only temporarily after removal of the hypophysis. Then, that the tuber cinereum, which alone of all the parts of the brain always contains a certain amount of the urine inhibitory hypophysis substance, shows even an increased quantity of the substance after removal of the hypophysis. In removing the hypophysis the pars tuberalis of the hypophysis, which is adjacent to the base of the brain and even enters into it, is not removed with it; it becomes hypertrophied, and the increta formed by it radiate now, since the posterior lobe is missing, to the gray substance of the base of the midbrain. It is therefore not surprising that with careful extirpation of the hypophysis, with especial care to preserve the base of the brain, polyuria does not develop. Furthermore, it is not strange that hypothalamic puncture remains effective in hypophysisless animals, since the increta accumulated in the tuber can no longer reach the ventricle, and especially the production of the increta in the pars tuberalis is badly damaged.

The recognition that the substance of the tuber cinereum is an incretion track and incretum accumulator, and that a vicarious part of the incretion hypertrophied organ is inseparably adherent to it, has badly shattered the arguments for the proof of the existence of an isolated water center, and with it also, the assumption that diabetes insipidus depends on affection of the nerve elements of the midbrain. At present, the pure endocrinal genesis of this disease is strongly supported. None the less, Frank is unwilling to deny some relation of the midbrain to the water output. Greving thinks that the tracts that go from the nucleus supra-opticus and perhaps also from the nucleus paraventricularis, through the stalk into the posterior lobe of the hypophysis, must indeed be assigned a functional importance. Frank believes that the midbrain-hypophysis system will have to be brought in relation with what is considered as the basis of thirst. Most likely, the entire substance of the ventral central gray matter is sensitive to the slightest withdrawal of water, especially the kind conditioned by osmotic hypertonicity of the blood, just as it is sensitive to changes in the temperature of the blood. This expresses itself on the one hand by stimulation of empty contractions of the esophagus, which according to L. R. Müller is an essential basis for the awakening of the sensation, and the taking in of water as caused by an imperative thirst sensation, and then again by the sending of impulses to the hypophysis, which with the aid of the increta make it possible to limit the elimination of water by the body.

Frank is inclined to believe that in threatened diminution of body fluids with nourishing substances essential to life, the midbrain reacts as it does when the water content is threatened. It is known that injection of insulin into a healthy person will develop a sensation of hunger when the fall in the blood sugar reaches

the level of being undetectable by test, and it is also known that hypoglycemia is brought about by the splanchnic activated by epinephrine, which brings on a too rapid mobilization of the sugar from the liver. One therefore comes at this point to an essentially vegetative activity of the midbrain composed of a subjective and an objective component, one of becoming conscious of a state of danger to the body through contractions of the vegetative organs, which sets in with false sensations, and again of calling on the organs of internal secretion to render such aid as they can in the emergency.

As regards the sugar and protein metabolism in its relation to the midbrain, it should be noted that Aschner often found glycosuria on puncturing the hypothalamus; this is occasionally found also in diseases of the base of the midbrain. F. H. Lewy, after injuring a circumscribed area of the vegetative oblongata nucleus (the dorsal vagus nucleus), observed retrograde cell degeneration in the nucleus periventricularis. According to Frank, these observations do not justify the assumption of a special center for sugar metabolism; they indicate only that in the field of general vegetative regulations, such as the increase of general metabolism by chemical heat regulation or by overcoming a deficiency of sugar due to any cause, perhaps also as a result of considerable excitations, impulses from the midbrain flow to the sugar metabolism center in the medulla. Aside from Claude Bernard's area, from which stimuli go to the liver and the suprarenals via the splanchnic, there is said to be a group of cells lying in its immediate neighborhood, lesion of which, according to Brugsch, Dresel and Lewy, produces hypoglycemia; these cells degenerate after extirpation of the pancreas. This is to be considered as most probably a vagus center.

Concerning protein metabolism, the work of Freund and Grafe is of interest. They have found that after sectioning the lower cervical cord there is a rise in the protein metabolism, therefore after a similar process which does away with chemical heat regulation; and Freund has further shown that this increase in protein metabolism also takes place when heat regulation center is being put out of use by large doses of antipyretics. It appears therefore that with this central apparatus there is closely associated another which exercises a subduing influence on the height of protein metabolism. These observations lead Grafe to explain the so-called toxic protein destruction in infectious fever on an intelligible basis. The marked protein metabolism observed under these conditions would therefore not depend on a peripheral attack of the toxin on the protoplasm of the cells, but would be rather the result of an injury to vegetative midbrain centers. One remarkable thing about it is that the bacterial protein should stimulate the temperature center while it paralyzes the "protein center."

Many are of the opinion that the hypothalamus plays a particular rôle in fat metabolism, in its deposition as well as its distribution. They believe that Frohlich's syndrome depends on an injury to the midbrain; they either entirely deny the hypophysis any participation or say that there are present in the hypothalamus, central regulatory organs that appear to be inactive unless it constantly receives stimulatory hormones from the hypophysis. On what is this nerve center assumption based, that it not only influences the metabolism but also acts on the mode of its formation and maintainance? In experimental lesions of the infundibular region, as well as in disease processes in this area, it is not infrequently observed that dystrophia adiposogenitalis and diabetes insipidus go hand in hand, and since the water center has been accepted as an established fact, the trophic center appears likewise established.

Bailey has called attention to the facts regarding cases of obesity and diabetes insidipidus. When the hypophysis is removed with great care, and injury to the base of the brain is avoided, accumulation of fat will not take place, but when in a secondary experiment the tuber is injured, fat accumulation will gradually develop. Since this experiment no longer substantiates a "water center" it appears natural also to question the existence of a "trophic center." Also, the arguments that in cases of dystrophia adiposogenitalis caused by tumor or hydrocephalus, the hypophysis is often found intact are not convincing, for in the infundibular region

the structures are so close in space that pressure on the hypophysis or on the conducting route may certainly block its increta. Even the adiposity following encephalitis may be considered as merely a brain symptom, since leptomeningitic changes extend to the stalk and to the posterior lobe of the hypophysis. Frank can see no valid reason for the assumption of a metabolism or a trophic generative gland center in the midbrain. Since, from the recent work of B. Zondek and Steinach, it was learned that the function of the anterior lobe hormones is that of a "motor of the sexual function," the assumption appears reasonable that obesity is the result of diminished generative gland function brought on by injury of the hypophysis.

It is to be recalled that the antidromically transmitted impulses from the sensory nerves for vasodilatation and tissue saturation can be realized only through the release of a chemical substance "histamine." How much more likely then, that growth, falling out of hair and loss of nails, hypertrophy and atrophy of the soft parts and bones, and changes in fat deposit and fat distribution which are observed after sectioning or on continuous stimulation of the peripheral nerves, or in diseases of the central nervous system, likewise take place through the intervention of a humoral agency, through a kind of locally developed secretion which first produces the trophic effect?

Apparently a humoral intervention will always have to be assumed in complicated processes. Some of the routes from the central organs to the incretory apparatus are now known; the secretory nerve of the suprarenal cortex is the splanchnic, the secretory nerve of the thyroid is the cervical sympathetic, of the pancreatic islands is the vagus; of the posterior lobe of the hypophysis is the tractus supra-opticus hypophyseus.

What portion under physiologic functional stimulation of the endocrine glands serves the central nervous stability is not yet clear, and indeed differs from case to case. Epinephrine output takes place preferably in association with sympathetic stimulation; the thyroid, the island apparatus and the hypophysis give off their indispensable increta for the regulated activity of essential organs of life, entirely independent of the nervous system. The midbrain, as a result of being highly sensitive to the slightest changes in the blood content, acts as a guard over the vegetative life, and at the first alarming signal acts through the endocrine glands—as, for example, in a threatening water diminution it acts through the hypophysis.

For pathology, Frank holds that it is very problematic whether the rôle played by the vegetative central apparatus is that of a driving or checking force in disease processes. Exophthalmic goiter, diabetes mellitus, diabetes insipidus and constitutional obesity are not neuroses or the results of loss of central functions. On the other hand, it is not to be doubted that powerful stimulation of the vegetative sphere of the midbrain may assume considerable importance as a result of the nervous connection between the midbrain and the organs of internal secretion for inciting and at times, for accentuating some of the diseases named.

It also appears likely that with growing age, somewhere from the fifth decade on, there is an increased tendency on the part of the vegetative apparatus to alterations which, when they reach a high degree, will result in a disease. "Essential hypertonus" should perhaps be mentioned in this sense; also prediabetic hyperglycemia of older people may be classed in this group. Two statements can indeed be made: (1) Nothing is known concerning localization; whether there is a changed tonus in the lower centers of the medulla, whether the midbrain should be held responsible, or one should accept Dresel and Lewy's hypothesis according to which the corpus striatum exerts a controlling influence over the midbrain. (2) It must not be forgotten that the so-called automatic activity of the centers depend on constant humoral stimulation: the H-ions stimulate the breathing center; choline acts as a hormone through its influence on Auerbach's plexus and brings on the rhythmic gastro-intestinal activity. It is thus likely, that the changes in the centers are due to hormonal stimulation. The tendency to arterial hypertension after ovarian activity ceases or after castration and in the climacterium,

may indicate that an alteration in the hormone equilibrium has taken place and is responsible for the apparent primary changes in the centers.

It is generally agreed that painful sensations from the abdominal organs and chest cavity are transmitted through the gangliated cord of the sympathetic. From animal experimentation by Neumann and Kappis (and Spiegel and Bernis, abstractor), it is learned that stimulation of the splanchnic nerve, especially the act of cutting it through, is accompanied by an unusual degree of pain, and Förster reports that electric stimulation of the splanchnic nerve brings on the severest pain which he has observed in man. The modern splanchnic anesthesia, which offers a painless abdominal operation, is based on the fact that after sectioning the splanchnic nerve, tugging on the intestines no longer develops pain. However, Kappis observes that this is not absolute proof of pain transmission by the splanchnic, since the vagus twigs that enter in the retroperitoneal ganglia and in the plexus, would be cut off. More effective is paravertebral anesthesia, which blocks the rami communicantes albi; not only does the visceral peritoneum become insensitive to artificial stimulation, but it also stops the violent pain of gallbladder and kidney colic; further, through relieving the pain in angina pectoris, it indicates that the transmission of pain for the chest cavity is also through the sympathetic. It is also generally accepted that the organs themselves are insensitive to mechanical, thermal and electric stimuli. Probably the afferent tracts which run in the sympathetic, enter the cord through the posterior roots. This conclusion is reached from the observation that after cutting the posterior roots, stretching and contracting produces no pain in animals. Yet W. Lehmann, on the basis of recent careful investigations, asserts that the sensory fibers of the splanchnic nerve run through the anterior root.

The question whether the afferent fibers of the gangliated cord and of the rami communicantes, which give information of the vegetative organs, belong to the vegetative or to the cerebrospinal system is merely academic. It can only mean whether they possess the same characteristics as the efferent sympathetic fibers, especially whether they are antidromically transmitting, identical with them. To be myelinated and enter through the posterior roots cannot be an argument against their classification as belonging to the sympathetic system; it is more important whether they, likewise through nicotine, enter the gangliated cord ganglion with interrupted synapses. This is substantiated by Brüning and Gohrband, Schiff denies it. The latter has also found that the rapidity of transmission in sensory nerves of the splanchnic corresponds with cerebrospinal and not with sympathetic nerves. An antidromic transmission in the gangliated cord, of the kind of axon reflexes leading to motor effects, was shown by Langley. In this way sensory stimulation perhaps may also reach central organs. If the sensory visceral nerves are not to be classed as belonging to the negative nervous system, they surely are to be classed as belonging to the unity of the vegetative system.

With the recognition that pain in the viscera is transmitted through the sympathetic tracts, it should in no way be denied that the vagus also plays an important rôle as a transmitter of sensations which are developed in the inner organs. Klee has definitely established that the act of vomiting is brought on through stimulation of the vagus fibers ending in the mucous membrane of the stomach. It is reasonable to assume that stimulation of the same fibers that form the centripetal shank of the subcortical reflexes, which precedes the act of vomiting, is responsible for the sensation of nausea. In favor of this conception is the observation by Förster that electric stimulation of the central vagus stump above the cardia produces definite nausea but no pain, and that mechanical stimulation of the intracranial vagus root brings on immediately a sick feeling and nausea without any complaint of pain, and that finally, after total sectioning of the cervical cord gastro-intestinal disturbances and the act of vomiting are always painless though nausea and a sick feeling take place.

Also, in diseases of the heart a sharp distinction should be made between the pain in angina pectoris, very often coming on entirely isolated, and the sensation of impending danger which in sudden, severe damage of the heart muscle

may reach an unbearable degree. Indeed, it is well worth considering whether here too the vagus is not to be considered as the transmitter of the specific organ sensation.

The localization of visceral pains appears to be diffusely spread. It gives the impression that for the inner organs there is only a thalamus sensibility and that they lack the discriminatory factor of the cortex. The old conception that pressure pain over the epigastrium is caused by stimulation of the solar plexus has again been accepted by Brüning, also that spontaneous abdominal pain depends on the same factor, especially the inferior mesenteric.

In subthreshold stimulation there is often only hyperalgesia of the dermatome of the same segment. Referred pain and hyperalgesia again point definitely to the transmission of pain through the sympathetic tracts.

For visceral pain, the contraction and stretching of the smooth muscles were made responsible. So far it has not been explained in what way long standing painless contracture, "hypertonus," differs from the painful contracture, "spasm."

It is especially difficult to get a clear conception as regards the origin of pain which is associated with abnormal conditions of the blood vessels. In attempting to explain intermittent limping as well as angina pectoris, many important possibilities were considered and many hypotheses were offered, such as spasm of the blood vessels, pain due to stretching and stimulation of the sensory nerves of the area with constricted blood supply by ischemia. Wenckebach has recently expressed himself against the prevailing teaching of "cramp of the coronary arteries." It is well known that the pain in angina (if cases of extreme pain depending on coronary thrombosis are excluded) sets in mostly on beginning bodily movements and forces the individual to stand still, as is the case in pain of the extremities due to peripheral arterial disease. Wenckebach accepts Pal's conception of "arterial congestion." In the beginning of a bodily exertion there sets in, physiologically, a kind of inhibition, which is felt as an anxiety, threatening paralysis of the bodily power; then relief comes suddenly and the execution of energy goes on undisturbed. This depends on the momentarily increased output of the heart, while at the same time there is an interference with the outflow due to arterial constriction. In a normal case this is quickly adjusted and the stretching of the aorta is not felt as a pain; when, however, the wall of the first part of the aorta is damaged or there is an involvement of the coronary vessels the stretching brings on violent pain which radiates to the lower cervical and upper thoracic segments. In addition to the abnormal sensitiveness of the sclerotic blood vessels, there is often added the more powerful interference with the outflow, since one is dealing with people with essential hypertension or near to it. Yet a solution of the problem is still lacking, because the violent pain reflexly supports the rise in the blood pressure; it is only through nitrite (which is incapable of lifting a coronary cramp), which opens up the peripheral block, that the pain recedes and the vicious circle is broken. The same mechanism holds good for intermittent limping. The postulated stretching of the aorta at the beginning of the attack was shown roentgenologically by Wenckebach.

Pathologically, the following groups can be distinguished: (1) Changes due to overstretching, perhaps also through permanent contraction, as for example in essential hypertension, when arteriosclerosis follows a functional state of many years, perhaps first only in those areas which do not take part in increase of the general tonus (kidney brain, coronary area). (2) The congestion in the hollow organs and canals through simultaneous weakening of the driving musculature and the contraction of the closing musculature, therefore through a repeated physiologic process which embraces the unity in the act of contraction of the wall musculature and the relaxation of the sphincters, as is observed in gallbladder inflammation with stone formation. (3) Necrosis caused by permanent ischemia; whether the arterioles and capillaries are themselves constricted or become closed from without through contraction of the smooth muscles through which they pass. Raynaud's disease, with gangrene of the fingers, is to be classed in this group.

Much effort has been expended in explaining the round ulcer of the stomach as a result of functional muscular and secretory disturbances. Experimentally, one can produce defects in the mucous membrane, even such as remain chronic in man. Erosions and ulcerations of the stomach wall have been described as the result of vagus stimulation, sectioning of the vagus and extirpation of the celiac ganglion. Gundelfinger has recently been able to produce ulcers of the size of a quarter by resection of the vagus and removing the celiac ganglion. Lesions of the thalamus, corpora quadrigemina, midbrain and neoplasms have been shown to have brought on chronic ulcers. For their immediate genesis either angiospasm or compression of the blood vessels through contraction of the muscularis propria or the muscularis mucosa are held responsible. O. Müller calls attention to the fact that at some distance from the gastric ulcer a vasoneurotic diathesis may also be observed, especially large varicosities with localized edema of the tissues. It is Allen's opinion that the diminished vitality caused by circulatory disturbances permits hyperacidity to attack the stomach wall. The hypersecretion and the hyperacidity, whether present primarily or as a result of the ulceration, contribute materially to the chronicity of the disease. According to von Bergmann, persons in whom ulcers develop are "vegetatively stigmatized" and as a result of a disharmony in the vegetative system of the stomach, tend to develop angiospasms, spasm of the wall and secretory anomalies. Frank is of the opinion that it is not advisable to completely set aside the relation to vagotonia as has been done by von Bergmann; perhaps many suffering from ulcer after all, belong to the pseudo vagotonic constitutional type, which is brought about by an alteration in the cation equilibrium. Kraus and Zondek consider that these local acidoses are a result of potassium ion increase in the periphery of the cell that is an expression of a pseudo-vagotonic constellation.

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Oct. 1, 1929

LOUIS CASAMAJOR, M.D., *President, in the Chair*

EMOTIONAL DETERIORATION IN SCHIZOPHRENIA. ITS MANNER OF DEVELOPMENT. DR. LELAND E. HINSIE (by invitation).

Time and circumstances are now favorable for a renewal of therapeutic interest in the management of schizophrenic problems. I shall here stress the treatment of the psychic (as opposed to the somatic) components, not because the somatic elements are less important, but principally because I prefer to consider one phase at a time. Several eminent investigators have already pointed the way to a rational form of psychotherapy. Since one cannot reasonably measure emotion without considering ideas or sentiments (as formulated by Freud, Prince, and others), I propose to elaborate on thought in schizophrenia. I have studied the patients in three cases of schizophrenia who met the following requirements: each was unquestionably schizophrenic; each was studied while in the incipient phase of schizophrenia; insight was present in each. Each patient was studied for at least one year, for no less than 100 hours. Investigation comprised the "free association" method along the lines set down by Freud.

As a result of these studies I have reached the following conclusions: Among thoroughly communicative schizophrenic patients (and there are many of them), emotional deterioration is only apparent, not real. There is no measurable loss of emotional capacity. What actually happens is a withdrawal of emotional interests from environmental situations and a subsequent reinvestment of the emotions to the service of the psychophysical self. Such a process was demonstrated to have taken place in the patients studied. With patience, industry and knowledge of the special technic (freudian), patients who still possess insight can

be appreciably benefited by being shown that a certain large share of the libido has remained attached to earlier (childhood) levels of adaptation. On the release of the emotions from the childhood anchorage, the patient is given an opportunity to apply the emotions to adult forms of behavior.

ENVIRONMENTAL FACTORS IN THE ETIOLOGY OF SCHIZOPHRENIA. DR. HARRY STACK SULLIVAN, Towson, Md. (by invitation).

The divergence as to the importance, respectively, of nature and nurture in the etiology of mental disorder in general and of schizophrenia in particular is susceptible of resolution by factoral analysis of a sufficient number of actual life situations. In carrying out this technic, one first distinguishes between the more or less transient phenomenology of schizophrenia proper and the more or less persisting phenomena indicating terminal processes following or arising in the psychosis. Incipient schizophrenia and true catatonic states are considered to be schizophrenia proper. The hebephrenic processes and the psychosocial dilapidation called praecox deterioration are one group of terminal processes, while chronic paranoid states are another. All the persisting persecutory states lying between the ideal poles of actual paranoia and utterly fantastic persecutory schizophrenic states belong here; most, probably all, are postschizophrenic conditions so far as the essential disorder is concerned.

Velocity of personality change may be taken as a criterion; from this point of view schizophrenia proper is of relatively high velocity and the terminal processes are of low velocity. Recovery, definable as the manifestation of adjustment processes sufficient for continued life in and within the patient's available social environment, too, is of low velocity; it is in a way a terminal process.

Duration in the sense of the partition of time in states of adjustment and of maladjustment is an uncertain criterion; any processes, presumably schizophrenic, regardless of duration, are relevant to this study. "Schizophrenic episodes" are more illuminating for study than are prolonged "kraepelinian typical" illnesses—this in part from our lack of acquaintance with the changes in boundary of the relevant environment in the latter. Such processes as those occurring in awakening from fear dreams are relevant. Incidents of panic in waking life are most important. In fact, there is a fundamental relation of panic episodes to the outcropping of schizophrenia. The wholly unexpected and sudden failure of anything important which has been implicitly accepted as wholly reliable; such is the general formula of the "cause" of panic. Panic is a primitive process; it is all but nonadjustive. When it occurs owing to collapse of some important adjustment relation of the self to other selves, a relation that has always been regarded as entirely dependable, the first great step toward schizophrenic disorder has been experienced. Unless the panic is promptly succeeded by adjustive or maladjustive processes that restore complete confidence in the self, a deviation of personality proceeds in the direction of a general insecurity in the cosmos; reality has, so to speak, developed an unreliability. Per contra, fantasy formations grow in valuation from dimming of the reality reference frames. The self world is disturbed and the personality integration dissociates more readily under pressure of conflicting impulses.

Schizophrenia proper seems to consist in the transcending of reality by fantasy processes under powerful drives; valuation is given to the content which results to such effect that common sense reality becomes more or less entirely illusory. This shows conspicuously in the field of valuation, including meaning which is vastly extended beyond the confines of true relevance in "external" reality.

Adolescence, defined as the last stage of personality development preceding the experience of sexual activity uncomplicated by powerful drives in conflicting directions, is the phase of personality growth in which schizophrenic illnesses can occur. In general, it appears that the sexual impulses are the only ones that culminate in situations necessitating an excursion into the schizophrenic psychosis. It appears that environmental influences that would teach realistic appraisals of the sex drives and their influence would prevent schizophrenic illnesses; the

teaching of a realistic attitude concerning the self (including the sex drives and their influence) is the obvious implication for mental hygiene in this field.

DISCUSSION

DR. A. A. BRILL: Dr. Hinsie followed lines that have been known to us. He presented interesting clinical material through which he tried to show that schizophrenic patients are not in as hopeless condition as one generally thinks; that incipient cases can be treated more or less successfully, and that through analysis one can unravel even the most complex neologisms, of which he gave instances. One has to work with the patient in order to understand the complexities of such productions. Dr. Hinsie recapitulated the works of the Zurich school in part with an effort to clarify the concept of emotions in relation to deterioration. In the Clinic of Psychiatry at Zurich similar efforts have been made with the aid of the galvanometer and the association experiments. Workers in this country have made similar contributions, but Dr. Hinsie's contribution is notable through his effort to explain the meaning of the term emotion, without which one should hardly speak about emotional deterioration. In this respect I learned from Dr. Hinsie that such seemingly divergent views as those of Prince and Freud nevertheless agree about the basic principles of the emotion. Having established this point, Dr. Hinsie cited his own experiences. When I think of my own experience with "deterioration" in schizophrenia, I recall a case I studied in the Clinic of Psychiatry at Zurich. The patient showed numerous neologisms and mysterious expressions. In discussing the patience and perseverance that one must use in dealing with schizophrenia, Bleuler told us of a patient with chronic catatonia who for years showed marked negativistic resistance. He wanted to move the patient from one sanitarium to another, and not caring to resort to the usual methods of procedure, he decided to use suggestion as he was much interested in the force of suggestibility in schizophrenic patients. Professor Bleuler actually talked to the apparently disinterested patient for a number of hours, suggesting all the time that she dress and come with him; finally, the patient dressed and for some time obeyed all his requests. I was much impressed by the experiment and decided to try suggestion on a similar patient, an American girl, born in Kentucky of Swiss parents, who had been brought from the United States to the hospital in Zurich after she developed schizophrenia. When I observed her she had already been there for a number of years. She was a typical catatonic patient who would sit with her face in her hands, her knees drawn up to her chest, never speaking or paying attention to anything. I selected her first because she was in a catatonic state and second because she was an American and I imagined that talking the English language to her might be helpful in the experiment. I talked to her continuously for about three hours, suggesting that she bathe and dress, and finally she obeyed and for three days she was perfectly normal. She answered all questions, giving a full history of the onset of the psychosis and cooperated in an association experiment. One of the stereotyped expressions she often used was something about "cement between the bricks." No one knew what it meant until I discovered that her malady developed after a love affair, in Kentucky, with a bricklayer with whom she had a disagreeable sex experience and this stereotyped expression was a sort of condensation of the whole psychosis. I could cite any number of similar expressions and neologisms if the time permitted. Thus for a few weeks I struggled with a patient with dementia praecox who in associating said: "phraser dirty beautiful Pekinese," which she herself could not understand. Thus far it resolved itself into the phrase, "Fraser, dirty but beautiful dog." On investigation I learned that a man with the name of Fraser had wanted to marry her, but was not of noble birth; also there was a Pekinese dog which was well bred indeed, but he was always dirty because her aunt did not want to give him a bath for fear of spoiling his coat. Fraser was thus identified with the dog; he too was handsome, well groomed, but he was too plebian and usually needed a bath. Similar condensations are frequently observed in dreams.

That schizophrenic patients have full insight there is no doubt in my mind, nor do they ever deteriorate in the strict sense of the term. One can always find the emotions. They may be deflected to something, but they can always be brought back if one tries hard enough. After three days of normal behavior, the aforementioned catatonic girl failed to come to my office, and the supervisor reported to me that she had returned to her former behavior. I did not have the courage to repeat the experiment in this chronic case. With patients having mild or acute schizophrenia it is a simpler process; if one works with them when they are accessible and cooperative one can often get as good results as in psychoneurotic patients. I thus agree with Dr. Hinsie that in such cases the prognosis is good. But one often obtains good results even in patients with chronic cases. At a meeting of the American Psychiatric Association I reported a number of chronic cases of patients who were treated by me analytically (more or less modified) who have made good adjustments and have maintained themselves now for many years. It takes a lot of time and a lot of patience to get good results, but it can be done. I am in full accord with what Dr. Hinsie said about the work still being in the experimental stage, but much has already been done by Dr. Hinsie and others to make a good start, which brings me to the second paper of the evening.

Dr. Sullivan has the capacity, I might say the schizoid capacity, to wax wittily and instructively about the nature and meaning of schizophrenia. Whatever he told us about the subject is entirely true I can assure you. His description and his deductions are based on a great deal of study and experience. There are few observers in this country who have devoted as much time to studying schizophrenic patients as Dr. Sullivan, so that his statements are authoritative. Still, a great many of his deductions are open to argument. Let us take, for example, his idea of the essence of schizophrenia that he finds with catatonic reaction. I can corroborate this in many or perhaps in most cases. Long ago I wrote a paper in which I said that all the infantile reactions to outer resistances are of a catatonic nature, and that the catatonic reaction was the earliest or most primitive reaction known to me. Therefore, I agree with Dr. Sullivan that catatonia is the most characteristic reaction in schizophrenia, but it is a question whether one should limit schizophrenia to the catatonic symptom-complex that is more or less present in many other psychotic conditions. Dr. Sullivan's idea of divesting schizophrenia of the superfluities that are not essentially of schizophrenic nature is stimulating. His classifications, too, are extremely interesting and well worth considering, but are open to discussion. Take the crash that he points to as a sort of precipitating cause and which he recommends for our experimentation. I happened to have had this experience in an aeroplane. I went into a military aeroplane and seeing the only seat there in the jack box, I naturally made straight for it. The pilot and observer were already in their seats, the motor was running and the plane was about to rise; as I walked to the seat I suddenly fell through the seemingly solid floor. I did not know that the whole center of the floor was an open rhomboid space merely covered with a piece of canvass. As I stepped on it, I fell through. In an instant I realized the situation and pulled myself back into the plane. I was shocked but not at all confused. The first thing that came to mind was, "Fortunately they had not yet started," and the next thought that flashed through my mind was, "Well, your heart is surely in good condition." I cannot tell you here the rest of the associations, but what happened was exactly what Professor Freud described in his theories of shock, fear and anxiety, in " Beyond the Pleasure Principle," namely, that following a shock the organism at once strives to bind the anxiety. One must not mind sacrificing oneself sometimes on the altar of publicity so I shall explain that some time previously I had had a cardiac attack for which I had been treated; and when I fell through the plane the mind made an effort to bind the free floating anxiety by assuring me that I was well; and for about an hour I continued with associations which were of the nature of grim humor, until I quieted down a bit and got over the shock.

I cannot say that such shocks or episodes are found in every schizophrenic patient that I have observed. I am now thinking, however, of the case of a brilliant young woman who showed no signs of schizophrenia until she had one of her ovaries removed; soon thereafter she withdrew from the environment and acted like a hebephrenic subject. I first saw her four years ago while she was in a sanitarium which she refused to leave. After considerable effort she was brought home and I treated her regularly for about two years. Although she maintains herself quite well, she has to be watched and must frequently be urged to go out and mix with people. This case seems to fit into the class described by Dr. Sullivan but I would add that this patient, as well as all the other schizophrenic patients studied by me, showed in the beginning a definite schizoid constitution. I feel, notwithstanding Dr. Sullivan's disregard for constitution or heredity, that whenever a shock such as he described is followed by schizophrenia one deals with a predisposed person. The father of the patient just mentioned committed suicide, and from the history obtained I think that he suffered from a manic-depressive psychosis. The patient herself showed manic-like moods even before operation took place.

The papers this evening impressed and pleased me. After many years one finds now and then thinkers like Dr. Sullivan and Dr. Hinsie who are undaunted by the kraepelinian hopelessness of dementia praecox and are working to bring some order out of chaos. Had it not been for the stimulating work of Freud, the approaches to the problem of schizophrenia would still be barren. It was Bleuler, instigated by Freud's work, who stimulated Jung and others to look with more hope on schizophrenia and from my own experience of over twenty-five years, I feel quite optimistic about the future.

Dr. George Van Ness Dearborn: What interested me most was the idea of a "redistribution" of the emotions and feelings in schizophrenia, and I wish to suggest that it tends to corroborate the late Prof. Morton Prince's concept of the "coconscious" and fits in nicely with such ideas. Of course, ideation is always present with the emotions because both are only aspects of the same process, and in at least 4,000 psychologic examinations for mental deterioration, which I personally have made, I think I can truthfully say I never saw one patient in whom intellectual deterioration was present when affective deterioration could not be observed. I am looking for both continually in my work, and certainly they always accompany each other.

I think it is easy to overemphasize the theory that there is "no real deterioration going on in the mind." In the first place, principles of habituation are active all the time, in which one gets into actual psychologic habits, and habit, continued after a long time in a negative way, leads at last to atrophy of a subtle kind. So I cannot go so far as Dr. Hinsie in postulating that there is no actual deterioration in schizophrenia.

I wish to ask your cooperation, when the time comes, in devising an apparatus for measuring the affects and emotions. It is one of the strangest things that this has not already been started systematically by a committee or commission including physiologists, neurologists, psychologists and psychiatrists. Prof. R. M. Yerkes was planning to make systematic efforts in this direction and I was to contribute my blood pressure studies on vasomotion in relation to affective and intellectual processes, prior to our entrance into the war. Dr. Yerkes, however, accepted such an excellent position in the army that he abandoned the research work and no one has taken it up since. It is assuredly within the easy possibility of present science to develop a system of some sort of measurements of physiologic, psychologic or neurologic emotion that would be more or less comparable in accuracy to the scales that we now have for measuring the intellectual aspects. It seems as though this should soon be taken up systematically by people interested in such matters and something done on it in a scientific way, without further needless delay. A scale for measuring feeling, as you all will agree, is one of the most urgent needs of psychiatry.

Dr. Gregory Zilboorg (by invitation): I should like to endorse most heartily the earnest attempt of Dr. Hinsie to study the finer details of the affective life of his schizophrenic patients. By way of corroboration of Dr. Hinsie's conclusions, I may mention the fact that a woman, aged 34, with a typical case of schizophrenia, who satisfied all clinical requirements of Dr. Sullivan as well as of the kraepelinian nosologic schemes, was treated analytically in Bloomingdale Hospital for a psychosis of four years' duration. Approximately 300 analytic hours were taken. The patient is now in her fourteenth month of normal life in a normal environment. In the course of the analysis she displayed essentially the same affective features as those which Dr. Hinsie described so well. Dr. Hinsie again made one aware of the fact that the most important step made in the traditional conception of schizophrenia was made by the psychoanalytic work that proved that dissociation of emotions has been mistaken far too long for an absence or "deterioration" of emotion. The classic concepts of Bleuler thus continue to be more in accordance with clinical psychopathologic facts than the traditional view which refuses to credit the schizophrenic patient with the full presence of affective values. The mistaken and only apparent disappearance of emotions in schizophrenia is but the extreme expression of the withdrawal from reality which was emphasized by Dr. Sullivan. The affects appear to go, but under proper conditions of therapy they reappear in their full freshness. Therefore, from the clinical therapeutic point of view it is important to bear in mind what Dr. Hinsie said when he spoke of redistribution rather than of deterioration of emotion. Our work in Bloomingdale Hospital on some schizophrenic patients appears to extend the validity of this view beyond the confines of the group of adolescent schizophrenic patients, for in our work we observed the same phenomena and arrived at the same conclusions in patients who were in their early thirties, middle thirties and close to forty.

I do not understand what Dr. Hinsie meant when he said that the schizophrenic patient withdraws the emotions from the outside world in order to concentrate them on his own psychophysical self. This explanation seems to me too general and too vague to be counted among the specific characteristics of schizophrenia, for the concentration of one's affects on one's own psychophysical self is equally characteristic of any deeply narcissistic pathologic state; the severe depressions may serve as an example.

At any rate, the old tradition of therapeutic hopelessness of schizophrenia, which was so convincingly attacked by Bleuler, seems to be breaking down as a result of systematic psychoanalysis.

With regard to the formulations of Dr. Sullivan, I think it is pertinent to emphasize once more the things which stood out in Dr. Hinsie's paper, namely, the schizophrenic manner of turning away from and then abandoning reality. Dr. Sullivan formulated this by means of a brilliant and somewhat different phraseology, but one is justified in recalling in this connection the classic description of this process in Freud's "Neurosis and Psychosis," which considers it the cornerstone of the problem of schizophrenia; whether the dramatic shock and the subsequent panic are necessary factors of the process cannot, I believe, be definitely answered, for the majority of schizophrenic psychoses are incipient and gradual. Nor is it quite clear why Dr. Sullivan finds it necessary to introduce the term empathy in order to explain the characteristic reactions of the child, the candidate for schizophrenia, to the restrictions imposed on him by the parents. Is not the amount of frustration and the psychic reaction thereto not so much dependent on the something which "flows from the mother" as on the amount of the something that is permitted or not permitted to flow from the infant, i. e., the amount of the libido that seeks expression and is dammed up after a frustration? It would seem that such an amendment would make the whole theory much clearer; moreover, it was rather well described by Freud many years ago; then, such vague terms as cultural conditions of schizophrenic states would become unnecessary insofar as they seem totally covered by the generally accepted view among psychoanalysts that the superego, bearer of cultural standards within the psychic apparatus of the

individual, is extremely rigid and uncompromising in the candidate for schizophrenia. The whole structure is so unassailable that continued and productive contact with reality becomes impossible.

Finally, the last point, it would be interesting to know why Dr. Sullivan draws the line of demarcation at the period of adolescence. Many adolescent persons develop schizophrenia, but to limit the beginning of the psychotic process to adolescence only means leaving out of consideration some important clinical facts that may not be overlooked. About twenty-five years ago, de Sanctis described dementia praecox in small children who undoubtedly had no time to reach chronologic, physiologic or psychologic adolescence. He called it then dementia praecocissima. In this country, some years ago, Dr. Brill described a group of cases in children whose reactions were typically schizophrenic responses to the Oedipus situation; in these patients too there is no doubt that they were on this side of the line of adolescence.

The criteria for evaluating the schizophrenic process still remains chiefly those that are outlined by the one who introduced the term, namely by Bleuler. The most characteristic of them is the splitting of the personality, the withdrawal from reality and its substitution by a set of projections fed by fantasy. To what particular period of the life this beginning of psychotic reconstruction occurs, one is hardly ready to say. I should say that the process is still so far so obscure and so intimately interwoven with the earliest part of the subject's psychosexual development that one cannot confine it only to adolescence or to any other special chronologic or psychophysiologic moment of adolescence. Apparently, it occurs in each person at a different period, depending on the particular life story in each case.

DR. C. P. OBERNRORF: The "traditional attitude" toward schizophrenia which has been emphasized tonight has not been quite so static as it would seem. As a matter of fact, the attitude of psychoanalytically investigating dementia praecox was established as long ago as 1909, at the Manhattan State Hospital. At that time the interpretation of the actions of schizophrenic persons in analytic terms and their symbolic significance was customary. As time went on, everyone recognized that the borderline, as Dr. Sullivan says, between schizophrenia and the neuroses is a fine one, that probably everyone is a bit schizoid, as well as neurotic, and that it is the degree of constancy that determines whether the person becomes schizophrenic in the pathologic sense. The normal person has transitory schizoid episodes.

On the basis of a minute investigation of the pathologic mental states, it became customary to decide whether a schizoid subject was suitable for psychoanalytic study on three bases: (1) the extent of the withdrawal from reality; (2) the persistence of clarity and insight, and (3) the degree of transference which can be obtained between the physician and the patient. In the analysis of schizophrenic patients I do not believe that the ordinary technic can obtain. The truly impassive attitude that the physician observes in the psychoanalysis of the compulsion neuroses will not work with the schizophrenic person who is bound to get libido to a greater extent from the analyst. Moreover, unless this libido takes tangible forms the chances are that the schizophrenic patient with a pronounced case will before long discontinue treatment. It has been my fortune to have analyzed two schizophrenic subjects, one man in 1912 and the other in 1910, and, on the basis of the analytic treatment, to achieve a marked readjustment to reality and the possibility of sustaining themselves well in the world. I can say that if a schizophrenic patient is put too quickly into contact with reality, his pathologic adjustment is disturbed, and it may happen that a long-sustained therapeutic treatment is annihilated quickly.

DR. CHESTER L. CARLISLE: It has occurred to me that as the peculiar behavior of the schizophrenic patient which makes him nonacceptable to society is due to dissociation or splitting of affect and ideation, that on the whole it would be much better to use the term "dilapidation," in the sense of dilapidation of personality, rather than "deterioration." One thinks of "deterioration" as associated with actual organic defects of neurons. If one uses "dilapidation" as referring to personality changes, it gives a little closer interpretation of the dynamics behind the complex

we are discussing. I suggest this for the sake of standardizing the terms of nomenclature so that we may all know exactly what we are talking about when we use certain words in describing these things.

DR. LOUIS CASAMAJOR: These two papers seem to me to be quite in line with the new psychiatry that offers so much of hope. Like Dr. Brill, I am one of the oldtimers, not so old as he, but still quite old, and I have seen psychiatry passing through three stages: the pre-Kraepelin, the Kraepelin, and now comes this new psychiatry to which it would be difficult to attach the name of any man, for it is still too general and too modern. Certainly it is giving a much better approach to mental problems and it is making psychiatry much more of a medical topic than it ever was before. Dr. Hinsie's conception of the so-called deterioration of schizophrenia seems to me to be well taken. I am always charmed with Dr. Sullivan's ideas which come as a breath of fresh air and frequently clear up a certain amount of the vagueness that is in my mind.

DR. LELAND E. HINSIE (closing): I wish to thank those who have participated in the discussion. Their remarks are helpful. I would add only that my contribution is little more than a correlation of the views of others. It is different in that it attempts to apply those views to the problems of schizophrenia, a task that has already been partly achieved by several investigators. My own views differ also in other respects, because I have leaned heavily on the early manifestations of schizophrenia. Jelliffe and Adolf Meyer have long since paved the way.

The main purpose of the contribution is to stimulate a therapeutic attitude toward the psychic components in schizophrenia. We have the means at our disposal, but because of the attitude of futility that has heretofore been held with respect to schizophrenia (or dementia praecox), this mental condition has not been given proper therapeutic attention. One must get away from the thought that all schizophrenic subjects are alike, or that they present a uniform symptomatology from beginning to end. For example, to say that lack of insight is pathognomonic of schizophrenia is not wholly truthful for all stages of the clinical picture. For a long time these patients possess as good insight into their abnormal manifestations as do other patients (psychoneurotic, for instance), who are known to be amenable to psychotherapeutic measures.

DR. HARRY STACK SULLIVAN (closing): I am somewhat overwhelmed at learning from Dr. Brill that I condensed "luetic" and "lutein" with telling effect. I should hesitate to face Dr. Zilboorg's evidence of my obscurity. It would once have crushed me, but I am beginning to wonder if it does not show only a healthy development of narcissism among those of us who work principally with the so-called narcissistic neuroses.

Te me, adolescence is not a "semichronologic period" in any sense whatever. I doubt that to refer to cultural conditioning is in any sense an offense of reason even though it may be an offense of good taste, in some quarters, in view of the extremely high degree of formulation which the analytic terminology has evolved. There are still a large number of people, and I presume some neurologists among them, who can use the term "cultural" as effectively as they can the term "super-ego." For that matter, if one must discover on every occasion that all human problems have already been solved, why continue to suffer voluntarily the spectacle of others' stupidity? Such, also, is my reaction to the reference to Bleuler's criteria. I regret that I have not found myself in agreement with Bleuler, but I have no quarrel with those who are in such agreement.

As to the dementia praecoccissima of de Sanctis, I cannot discover it. I have asked my friends to inform me if they should see any case of schizophrenia occurring before the appearance of normal homosexual interests at the close of the juvenile era, and no such case has come to my attention. I once thought the de Sanctis' dementia praecoccissima would be the negative instance disproving my theory of schizophrenia, but having failed to see it in our native born patients I am now inclined to discount it on the basis of cultural and racial differences in de Sanctis' material.

As to Dr. Brill's children, I think that this material is in keeping with the hypothesis I have tried to lay before you. I think that his material would demonstrate the preceding uncertainty about the self-world synthesis and that it was on this background with the coming of the sex impulse that schizophrenia made its appearance. Schizoid phenomena cannot yet be distinguished in the mental life of early childhood; schizoid mental life is probably outgrown in later childhood or early in the juvenile era.

As to Dr. Brill's most kind remarks, I can but say that I think it is the overcondensation of my presentation which leads to his difference of opinion as to the break in the self-world synthesis to which I referred. I think that this event that I allege will be found of great importance in the understanding of schizophrenia. As to the schizoid-manic formulation, it is beyond the scope of my remarks this evening. One certainly observes many excitements in adolescent persons that look manic but prove to have a deepening schizophrenia.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Regular Meeting, Oct. 8, 1929

MOSES KESCHNER, M.D., *President, in the Chair*

PATHOGENESIS OF MULTIPLE SCLEROSIS. DR. RICHARD M. BRICKNER.

This paper will be published in full in a later issue of the ARCHIVES.

EXPERIMENTS ON DEMYELINATION: THE IDENTITY OF HEMOLYSINS AND MYELOLYSINS. DR. ARTHUR WEIL.

In a study of the effect of anemia on the spinal cord (Weil and Davison: ARCH. NEUROL. & PSYCHIAT. **22**:966 [Nov.] 1929), support was given to the theory of other investigators that in pernicious anemia one and the same toxin acted destructively on the hematopoietic and the nervous system, although both might reveal themselves clinically at different periods. Based on this histologic research, the idea was conceived to investigate the effect of hemolytic toxins on nerve tissue.

Representatives of four different groups of hemolytic toxins were chosen: saponin, sodium taurocholate, cobra venom and streptolysin. In test tube experiments with spinal cords and solutions of these toxins it could be demonstrated that all of them acted destructively on the myelin sheaths of the nerve fibers. In Weil-stained sections a peripheral zone of demyelination was seen which increased in size with the concentration of the toxin applied. In quantitative experiments the amount of saponin which was bound by 1 Gm. of spinal cord in different concentrations was determined. This amount was calculated by comparing the hemolytic effect of the solution at the end of the experiment with that of a standard saponin solution. It could be shown that the amount of saponin which is bound by 1 Gm. of spinal cord increases with rising concentrations. At the same time it appeared likely that this process of saponin absorption to the nerve tissue resembled in its mechanism the absorption of the hemolytic amboceptor by red blood cells. Another similarity between the process of myelolysis and hemolysis was demonstrated by the influence of lipoids on the action of saponin. In both instances small amounts of lecithin (one part to one part of saponin) did not influence the two processes, but addition of large amounts (five parts of lecithin) inhibited both hemolysis and myelolysis. Brain emulsions acted in a similar way.

The neurotoxic action of the four hemolytic toxins and the lipoid-saponin combinations was always related to the myelolytic effect. The more pronounced

the demyelination the more intense was the toxic effect as tested by injections into white rats.

The liberation of hemoglobin in the process of hemolysis is made possible by the dissolution of the stroma or pellicle of the red blood cells which is supposed to consist of lipoids mainly. In a similar way, the dissolution of the myelin sheaths is brought about by the transformation of the lipoids of the myelin sheaths into soluble combinations through the action of the hemolytic (myelolytic) toxins. From all these observations it was concluded as a working hypothesis for further research that animal and bacterial toxins which at the same time produce hemolysis and myelolysis and which act as neurotoxins do not contain different principles, but that one and the same substance produces the different physiologic effects. Its action is dependent on the amount and kind of lipoids present in the solvent of the toxin and in the different tissues on which it acts.

DISCUSSION

DR. LEON H. CORNWALL: It has been my privilege to follow the work of Dr. Brickner and I know that he has exercised infinite care in technic and has controlled his experiments with an adequate number of normal cases. The results may be summarized by the statement that when sections of the spinal cords of rats are placed in blood plasma from patients with multiple sclerosis there is an alteration in the physical state of the myelin that cannot be duplicated by similar treatment with the blood plasma of patients without multiple sclerosis. The process is one of myelinolysis. The physicochemical processes involved are far too complicated to warrant any attempt at explanation at the present stage of this work. The quantitative and qualitative differences observed when the blood plasma of patients with multiple sclerosis and normal persons was used constitute a fact susceptible of confirmation by other workers.

The composition of myelin probably includes all of the lipins, which is a very large group. The individual constituents consist of fatty acids, cholesterol, cholesterolesters, phosphorus, a carbohydrate group, nitrogen, sulphur and inorganic salts. According to the molecular constitution, the lipins have been classified as galactolipins or cerebrosides (cerebrin, phrenosin, kerasin), phospholipins or phosphatides (lecithin, cephalin, sphingomyelin) and sulpholipins or sulphatids.

Normally, myelin is in a stable physical state. In all probability, protein is the constituent that is largely responsible for the normal stability of myelin, although soaps and carbohydrates also act as stabilizers. Marinesco has expressed the opinion that amyotrophic lateral sclerosis is due to a process of autolysis produced by endocellular ferments, and that these endocellular ferments perform two functions, catalysis and oxidation or hydrolysis. In his opinion, myelin degeneration is an expression of hydrolytic activity which results in the conversion of lecithin into stearic and glycerophosphoric acids and choline.

Although the facts that have been presented do not clarify the various physical factors that are concerned in the destruction of myelin, they are a step in the right direction and further study may lead to a more accurate knowledge of the causation of the disease, and finally that goal, which all would like to attain, a successful method of therapy and prevention.

The details of Dr. Weil's paper are too intricate to warrant a discussion unless one has studied it carefully. They represent a well conceived and well done piece of work. In one particular, both Dr. Brickner and Dr. Weil discovered the same thing, namely, that immersion of the spinal cords of rats in physiologic solution of sodium chloride produces a tremendous distortion of the myelin sheath, without actual myelin destruction. The fact that normal plasma produced a considerable alteration of the physical state of myelin is important. I think that it gives perhaps a lead; it gives a right to postulate that in the blood of patients with multiple sclerosis, there may have occurred an alteration in the relative amounts of substances that normally are present.

The reduction of the hemolytic action of saponin by the addition of lecithin was also interesting to me, because lecithin is one of the phospholipins or cere-

brosides consisting of fatty acid, nitrogen and phosphorus. One might perhaps be warranted in attempting to ascertain just which one of the three radicals is concerned in the inhibition of the hemolytic activity of saponin. Is it fatty acid, nitrogen or phosphorus? That is a problem which doubtless could be determined easily.

The demonstration of the action of saponin on the hemoglobin and not on the stroma of the red blood cells was also illuminating to me and might suggest the explanation of a fact that I noticed in some experiments on myelin a year or two ago. In prenatal and very young animals I described globular forms resembling, morphologically, red blood cells but not corresponding to the latter in tinctorial reactions. They were present in the fourth ventricle, subarachnoid space and periphery of the neuraxis. In a rat, twenty-four hours after birth, these globular forms appeared to be passing from a vascular sinus in the pia-arachnoid directly into the periphery of the spinal cord. The globules stained black with the Weigert-Pal stain, but with other stains they did not give the reaction of red blood cells. Is it possible that in these young animals certain of the normal adult constituents of hemoglobin are absent: possibly iron, possibly phosphorus or possibly manganese?

THE REFLEX ACTIVITIES OF A DECEREBRATE ANIMAL. DR. LEWIS J. POLLOCK and DR. LOYAL DAVIS.

The sum total of all of the reflex activities residing in a decerebrate animal produces the posture of a caricature of standing and the distribution of overwhelming extensor tone in the antigravity muscles. Each of these reflex activities is integrated with the others, some facilitating, others inhibiting or masking one or another. Marked decerebrate rigidity in extension may be elicited by labyrinthine stimuli in partially decerebrate animals which under other conditions can run, jump, crawl or have normally distributed tone. Removal of the labyrinths of a decerebrate animal is followed by a lasting pattern of flexor rigidity in the fore legs, whereas the hind legs are still rigidly extended. When the reflexes of the neck as well are destroyed by section of the first, second, third and fourth cervical posterior roots, the distribution of tone in the fore legs is equally distributed between the flexors and extensors. The extensor tone still predominates in the hind legs but is far less than in either the decerebrate or the labyrinthless decerebrate animal. Thus it is seen that different patterns of tone are formed by each of the reflex activities. Not only do these several reflex activities determine by their interrelation the general posture of tone, but each one modifies the reflex activities of other reflexes, both nociceptive and proprioceptive. The preponderance of flexor or extensor tone determines the activity of antagonistic muscles, so that, in a flexor nociceptive reflex producing co-contraction during a state of increased extensor tone, a contraction may be observed in the antagonistic extensor, whereas such a contraction is absent if flexor tone predominates. Tonic reflexes, such as neck and labyrinthine, tend to show reciprocal innervation with relaxation in the antagonist. Such a reflex is frequently preceded by a nontonic reflex showing co-contraction. The cerebellum exerts an inhibitory action over the labyrinthine reflexes, and when it is removed in a decerebrate animal excessive labyrinthine reflexes can be evoked.

DISCUSSION

PROF. F. H. PIKE: Hearing about the effect of saponin on blood corpuscles and the effect of ligation on the cerebral arteries has taken me back some years to the time when I was in Chicago working with a good, hard-headed Scotchman, C. N. Stewart. At that time, also, Waldemar Koch was working on the chemistry of the brain. Unfortunately, Koch died of pneumonia, but I have had the feeling for the past twenty years that I would like to see someone else seriously attempt a study of the chemistry of the brain. I think that the need for such study was brought out by the mention of the galactolipins and phospholipins. However, at that time in Chicago there began perhaps my departure from the faith, so far

as neurology was concerned. The experiments with ligation of the arteries to the head made me skeptical of the whole hypothesis of shock and inhibition. It did not seem as if you could put together any mechanism which worked on those principles. Really, inhibition began in Russia and became incorporated in the German texts; shock has a somewhat similar history, and I have never seen a clear statement of the exact meaning of either shock or inhibition. I am not saying this because these gentlemen are here. I should far rather not say it.

There is, I think, no overestimating the importance of such work as Dr. Pollock and Dr. Davis have been doing from the standpoint of clinical diagnosis. It is going back to that old program of Pourfour de Petit, two hundred years ago and more, who thought that he would like to duplicate by experimental procedures those conditions which he encountered clinically in the nervous system.

I will say that back in Chicago there began this lack of faith in shock, inhibition and in the whole segmental hypothesis of the nervous system. The argument has been made that, since recovery is possible after a lesion of the pyramidal tract, for instance, the pyramidal tract does not have much to do with voluntary movement. If that argument is pushed to its extreme, one meets a discouraging prospect. There is little in the cerebrum which cannot be dispensed with at one time or another, and one begins to wonder why the cerebrum was ever developed. The prospect seemed too pessimistic. There is no need to tell the devious paths I followed until I found right before me facts that have been in the literature for years wholly neglected for purposes of interpretation, and those data have to do with experimental lesions of the spinal cord.

It has been known for many years (Pike, F. H.: *Am. J. Physiol.* **85**:400, 1928) that when the spinal cord of an animal is hemisected in the thoracic or upper lumbar region, after a brief interval of a few days movement returns in the hind limb on the side of the hemisection. Let us apply Goltz's remark, concerning transection of the spinal cord, that since the reflex functions returned in so short a time, no one would assume that the spinal cord had acquired any new functions. One must assume that they had been only temporarily suppressed or inhibited. If that is true, then that isolated portion of the spinal cord lying below the level of the hemisection is the only thing that is needed for movement, and none of the descending tracts going down there (pyramidal or rubrospinal) nor any of the ascending tracts coming up from there are necessary. That is Goltz's argument, of course, pushed to its limit. I do not believe that that lower portion of the spinal cord lying below the level of the hemisection has within it all the mechanisms that are necessary for voluntary coordinated movement.

Hughlings Jackson (cited by Sir Victor Horsley: *Brit. M. J.*, April-June, 1907, p. 803) had anticipated me in the explanation of that. Jackson had the idea that after a lesion of any particular system there is a change in the quantity of the nervous energy flowing through the remaining systems. It seems to me reasonable to suppose that after hemisection of the spinal cord, something going down, perhaps on the other side, has taken on an additional burden of function, taken over the control of the movements of the hind limb on the side of the hemisection. That is the only way I see out of it. And there is a good deal of other evidence, which I have accumulated, tending to show that after the injury of any one pathway there is a change in the functional capacity of some other pathway associated with that particular function.

Going back to the pyramidal system, our ideas of its function are based pretty largely on the deportment of animals after a lesion of the pyramidal system itself. In the higher forms one may get rigidity, or spasticity of the limbs, when the lesion does not go very far below the cortex. In common laboratory animals (the dog and the cat) it is necessary to go well below the cortex and get down fairly close to the midbrain before the typical spasticity develops.

If the pyramidal system has little to do with voluntary movement, and if this movement is negotiated by mechanisms in the midbrain, it ought to be possible to leave the pyramidal system intact and make some lesion in the midbrain which should produce a severe and permanent disorder of locomotion. It should be

possible to eliminate, practically complete, the rubrospinal system and leave the pyramidal system intact. It should be possible, for instance, to make a median incision in the midbrain which would sever the decussation of Forel and the decussation of Meynert, and give a bilateral lesion of the rubrospinal pathway (Pike, F. H.; Elsberg, C. D.; McCulloch, W. S., and Rizzola, A.: *Am. J. Psychiat.* **9**:271, 1929). I have one such animal in the laboratory now; that is, I would not say without postmortem examination that I have cut those two decussations, but I have tried that same thing on other animals and in looking over some slides of degeneration today there is extensive degeneration in the region of the midbrain (Marchi preparations), and I have not seen any in the pyramidal tract. Yet, strange to say, that animal was able to walk about very well. If the pyramidal tract has nothing to do with voluntary movement, then by the same token, since the animal recovers after a lesion of the rubrospinal tract, that ought not to have anything to do with voluntary movement. So one must look somewhere else — perhaps in the medulla. However, such a conclusion does not seem reasonable. It seems far more reasonable to apply Hughlings Jackson's idea that after the lesion of any one pathway or system there is a change in the functional capacity of some other pathway or system associated with it.

When one looks at the nervous system from such a point of view, it does not in the least minimize the clinical importance of the work of Dr. Pollock and Dr. Davis, but I think that it does modify somewhat our conception of the normal reflex and other activity of these mechanisms in the midbrain.

Some years ago, I was interested in the question of vestibular reflexes, nystagmus and the like. I found that I was not getting anywhere. I could not put together, in terms of nerve impulses and fiber tracts, a machine that would work. So I left that and started on the respiratory mechanism. I think that now I do have some idea of how a mechanism is put together and how it works. I think that I can see the significance of the midbrain in respiration. Very little of that has been published, in fact, only the briefest notes (Pike, F. H., and Coombs, H. H.: *Science* **56**:691, 1922. Springer, M. G.: ARCH. NEUROL. & PSYCHIAT. **19**:834 [May] 1928). Some day I hope to get it together, when the facts are complete enough. Just one instance from that system to show what I mean by a change in the functional capacity of the conduction pathways. It has long been known that if both vagus nerves are divided in the neck, the immediate effect on respiration is a great reduction in rate, the rate falling to one-half or even less the regular rate. After a few weeks, that rate may return practically to normal. Following Goltz's argument, one would say that the vagus had little to do with the control of respiration. I shall let it go at that for a moment. When the dorsal roots of the thoracic and cervical regions are divided, the costal movements of respiration cease. I do not know how long such a condition lasts. I have asked a number of neurologists what the condition of the respiratory mechanism is in tabes which is far advanced. That seems to be a point of clinical observation that has escaped attention.

If any of you encounter a tabetic patient in whom degeneration has extended up and involved the dorsal roots of the thoracic mechanism, I should like to know what the costal movements in such a patient are. I would not expect much change.

There are apparently two mechanisms, the vagus and the dorsal roots of the thoracic nerves, lesion of either one of which will produce a change in respiratory activity. When there is a lesion of both at the same time, the respiration gets extremely bad and the animal does not survive very long.

If the vagus has nothing to do with the control of respiratory movements, it ought to be possible to cut the vagus, allow the animal to recover and later on section the dorsal roots of the thoracic nerves without any severe effect. However, no matter what interval has been allowed between the section of the vagus nerves and the section of the dorsal roots of the thoracic nerves, the final effect has been just as severe as if it were done on the same day. Apparently, the dorsal roots are capable of taking over some overload of function after injury

to the vagus and apparently there is nothing else that can do so. There are the two afferent pathways which are normally concerned in the control of such a movement as respiration. After a lesion of either one of them, a considerable degree of recovery is possible. I do not believe that recovery is possible after a lesion of both.

It seems much simpler to regard this pyramidal and extrapyramidal system from some such point of view than as a system of mutually inhibiting mechanisms. If all the inhibition which is supposed to occur went on, I do not see how one would ever reach any conclusion. I do not see how the brain could get anything done if it were continually inhibiting itself; and yet a great many things are done.

Again, in the animal which I now have in the laboratory, which has lived for three months, I should say, since section of the median section of the midbrain, that there is considerable spasticity of all the limbs and some spasticity of the tail; the gait is goose-step; the fore and hind feet are raised high as the animal goes back and forth on sentry duty. I think that the pyramidal tract is wholly intact there. If it were inhibiting any such spasticity, it should inhibit it. It has not done so in this animal.

I will admit that this has not much to do with the paper presented; it probably has little to do with clinical neurology as it is conducted at present, but I think that eventually it will have some relation to our interpretation of the results of lesions of the central nervous system and with our view of the nature of the return of function, or as Hughlings Jackson spoke of it, "the compensation for lesions of the central nervous system."

I wish only to commend Dr. Pollock and Dr. Davis for carrying on work which I did not have the nerve to continue myself, and I would again emphasize its value to present-day clinical neurology.

DR. HENRY ALSOP RILEY: I have no contribution to make to the scientific aspects of the subject which Dr. Pollock and Dr. Davis have placed before us, for I have had no experimental experience with these investigations. I think that without question this paper is the best piece of technical investigative work which I have heard presented certainly before the section, and I think that I can say before the American Neurological Association. It has been a pleasure to listen to the results of such careful, accurate and beautifully executed procedures and observations.

The question of tone, up to the present time, has been principally the battle ground of the English, Dutch and German schools, but during the past few years an increasing number of contributions have come from Chicago, from Dr. Ranson who is associated with Dr. Pollock and Dr. Davis in the Department of Neurology and from Dr. Pollock and Dr. Davis and I feel that in the future much more of value will be contributed to this study by the American School than has been up to the present time. I know that these men will be the chief protagonists in such contributions.

Just as a personal plea I wish that someone—and I know of no investigators better qualified than those whom I have mentioned—would sometime put together a description of these functions and neural mechanisms which go to the maintenance of tone and the production of these phenomena without all of the technical detail. To one unfamiliar with these procedures, that is, the experimental methods followed, it is difficult to keep in mind the exact object and trend of the entire investigation.

I know that on a number of occasions I have heard Dr. Pollock present these studies on tone and I have been able to follow him for some little time and then I have been led off into one path or another and lost the trend of the argument entirely. I think that probably a number of others have been in the same position. Therefore, if he could put together the ideas, the principles and the conclusions without so much of the actual procedures, I know personally that I would have a much clearer conception of the problem of tone and the neural mechanisms invoked.

I think that we cannot let this evening close, as Dr. Keschner has already mentioned, without expressing to Dr. Pollock and Dr. Davis the thanks of the

Section of Neurology and Psychiatry of the New York Academy of Medicine for this remarkably interesting and painstaking presentation.

DR. LOYAL DAVIS: I can only express my pleasure at being here and say that I at least can understand the difficulty which Dr. Riley and Dr. Strauss have in understanding a thing which we have battled with for about eight years and only now perhaps can talk to one another about in rather simple terms.

DR. LEWIS J. POLLOCK: I am sure that Professor Pike did not mean to state that he understood me as saying that the pyramidal tract had nothing to do with voluntary movement. That, of course, was far from my intention. I am agreeable to try sometime to express our points of view in a simpler form, which we will probably find to be difficult.

I wish to take this occasion to pay tribute to Dr. Davis' exceptional surgical skill, without which none of this work would have been possible.

Book Reviews

REPORTS OF THE COMMITTEE UPON THE PHYSIOLOGY OF VISION. IV. EXPERIMENTS ON BINOCULAR VISION. By N. M. S. LANGLANDS. Medical Research Council, Special Report Series, No. 133. Paper. Price, 2s.6d., net. Pp. 69, with 34 illustrations. London: His Majesty's Stationery Office, 1929.

Binocular vision has been much discussed for many years. Ophthalmologists, physiologists, anatomists and psychologists have all, at various times, worked with it and disagreed always. Theories have been evolved not so much to explain binocular vision as to fit a problem on which the theorist might be working. It has been the exception for any one person to confine himself absolutely to it, per se, and attempt to clear up some part of this complex mechanical, physiologic, psychologic and anatomic function. Wheatstone, Donders, Hering, Heine, Helmholtz and more recently Parsons were some of the outstanding investigators to develop workable theories for this function. Most of the present-day understanding of it is due to them.

The Medical Research Council, in the reports of the committee on the physiology of vision, have published section IV, Experiments on Binocular Vision, by N. M. S. Langlands (Medical Research Council, 30 Old Queen Street, Westminster, S. W. 1), sixty-nine pages, June 18, 1929. The report contains the results of a series of studies on binocular vision undertaken during the last few years at The Royal Naval College, Greenwich, by Instructor Lieutenant-Commander N. M. S. Langlands, R.N., M.A., D.Sc. It is an original work of great scientific value published by the Council on the recommendation of Commander Langlands and by permission of the British Admiralty.

The author subdivides the thesis into four parts: Part I, Introduction; Part II, Experiments on Binocular and Vernier Acuity; Part III, Measurement of Binocular Acuity for Small Illuminated Disks in a Dark Field; Part IV, Experiments on the Effect of Variation of the Duration of the Illumination on the Binocular Acuity.

In this report, the author has taken the subject of binocular acuity and vision and worked with it as a purely academic entity as the chemist would work with a new element to determine its reactions, its acids and salts, its densities, weights, its morphology, etc. He has described more than thirty different experimental methods used in this detailed investigation of the subject.

The introduction deals with an explanation of binocular acuity, the three methods of measuring it and a brief historical summary of the recorded results of Helmholtz, Stratton, Bourdon, Frübose and Jaensch working together, Pulfrich, Hering, Heine, Crawley, Brooksbank James and Howard, Anderson and Weymouth, Tschermak and Kiribuchi, and Fischer. He points out in comparison that this measurement of acuity is in terms of resolving power. As the acuity of an eye is the minimum angle between two points the images of which are just capable of being separated, so is binocular acuity determined as the minimum resolvable difference in depth, and is measured by the smallest difference in binocular parallax which can just be appreciated. The introduction outlines also the work on binocular vision and acuity using momentary illumination and constant illumination and the measurements of binocular acuity with instantaneous, momentary and constant illumination. In addition, the binocular acuity in indirect vision with the electric flash and binocular acuity with the stereoscope and its persistence with the stereoscope are considered in detail.

Part II outlines thirteen experimental methods on binocular and vernier acuity. In this, momentary and constant illumination are used, with and without a Stratton pseudoscope. The author's conclusions on this section enable him to eliminate such causes as the size of the retinal images and to state that for constant illumination both the binocular and the vertical vernier acuities gave a 50 per cent threshold of about five seconds. For very short flashes which cannot involve ocular move-

ments a fairly high instantaneous binocular or vernier acuity can be reached by practice. One of his observers attained a 50 per cent instantaneous binocular threshold of ten seconds, while his best 50 per cent instantaneous vernier was a bit larger.

Part III considers measurements of binocular acuity for small illuminated disks in a dark field. In this nine different procedures are outlined including work again with the pseudoscope and with synopters, and with disks of different colors. Work was also done to determine, if possible, the influence of peripheral stimulation on binocular acuity. The conclusions presented at the end of this section are such as to allow the author to state: (1) that as the angular distance between the center and the wing disks increases (up to 4 degrees) the binocular acuity diminishes for a moderately dark-adapted observer in much the same way as the visual acuity diminishes, (2) that peripheral stimulation exerts a disturbing influence on binocular acuity and (3) that he has been able to outline a new theory of binocular vision based on the photo-electric theory of light. This theory is given in detail.

In part IV the effect of the variation of the time of action on the light flash on the binocular acuity is investigated. These observations were made under two different conditions, first when the diameter of the field and the duration of the flash were unknown (taken at random) and second, when the duration of the flash was known to the observer and the observer had acquired experience by consecutive observations with this duration. As a result of this investigation the author can make certain logical conclusions of great scientific interest. It is evident from them, he states, that "the variation of the binocular acuity is dissimilar from that of the variation of the sensation-intensity, and that it cannot be explained in terms of total sensation." Further, the possibility of binocular acuity by convergence with ocular movements is fairly debated. Lastly, the physiologic side of the matter is correlated with all possible elements capable of modifying it into a working hypothesis.

A remarkably complete bibliography closes this presentation.

A Practical Treatise on Disorders of the Sexual Function in the Male and Female. By Max Hühner. Third edition. Price, $3. Pp. 342. Philadelphia: F. A. Davis Company, 1929.

This book by Dr. Hühner is well organized and clearly written. Under the captions etiology, pathology, symptoms, prognosis and treatment, the author states in each chapter the main facts of the disorders included. Each section is made complete in itself. The book deals with masturbation, impotence, pollutions, priapism, satyriasis, nymphomania, frigidity, vaginism, absence of orgasm, enuresis, withdrawal, continence and dysmenorrhea. It seems necessary to take issue with the author's opinions, which are at variance with a great deal of what modern psychiatry teaches concerning these conditions, both theoretically and practically.

Dr. Hühner expresses definitely his opinion that the so-called sexual neuroses and allied conditions are for the most part due to local organic disorders. Accordingly, "the treatment of sexual neuroses belongs to the genito-urinary rather than to the neurologic specialist" (page 5). Throughout the book the psychogenic aspects, the important psychosomatic interrelations and the value of psychotherapy are greatly neglected. Although the author gives credit to Freud for important work on sexual neurasthenia, one might almost think that he considers psychoanalysis a disease, as when he says: "I will not discuss such conditions as psychoanalysis or the various forms of sexual degeneracies or perversions. These belong strictly to the neurologist, as their pathology belongs rather to the field of abnormal psychology than to the genito-urinary apparatus" (page 9). Most emphasis is put on local congestions of the verumontanum, that ever-present Oedipus complex of genito-urinary specialists. A full page illustration, giving a rather simple diagrammatic illustration of the verumontanum — normal, moderately enlarged, very enlarged and atrophic — is printed twice (on pages 93 and 230). Local congestion of this region, we are told, is one of the most important factors in

masturbation, sexual neurasthenia, impotence, satyriasis, etc. Local instillations of silver nitrate into the posterior urethra are recommended almost as a panacea for neurotic disorders in the sexual sphere. The author explicitly states that he believes this to be a specific remedy against the underlying pathologic conditions, and not a psychotherapeutic influence. The reviewer feels that it is his duty to state, from a large experience with cases of this type, that in nine cases out of ten of so-called sexual neurasthenia such local applications are a mistake, because the seat of the disorder is not a local congestion but a personality disorder which has to be attacked by appropriate methods. Sufficient weight is not given to the important symptom of anxiety in the conditions treated. The division into autonomous chapters, while adding greatly to clearness, gives the wrong impression that neurotic sexual disorders can be sharply differentiated in their symptomatology and treatment. If the medical reader will derive any profit from this book, he has to take it with a grain of salt, and with the realization that the author overrates greatly the rôle of local organic conditions.

It is not possible in the course of a review to take issue with the details of each chapter. But the first three chapters, dealing with masturbation, disagree to such an extent with the tenets of modern psychopathology that they have to be specifically discussed. The author retains the terms masturbation and onanism, believing that "long and common usage" compels us to do so. The term autoerotism, however, is more accurate and in common usage in psychiatry today. He regards this condition specifically as a "disease." Particular exception has to be taken to the pernicious advice which Dr. Hühner gives with regard to the detection of this "disease" in young boys. "The physician should not neglect an examination of the genitals in any suspicious case, and very often the local symptoms will tell the tale. In young boys, after an examination of the genitals by the physician, whether he finds anything there or not, it is often advisable for the physician, if he is reasonably sure of his ground from the general symptoms, to tell the boy immediately after the examination that he masturbates. The boy, being taken off his guard, if guilty, will imagine that the physician can tell by the examination, and will often admit the truth at once" (page 6). Is there a surer method of starting a serious hypochondriacal reaction in an adolescent—or an adult, for that matter—than by giving him the (wrong) impression that he has injured his genitalia by masturbation to such an extent that a physician can detect it at sight? Unfortunately, such methods are frequently employed. In a recent case of the reviewer's experience, similar procedures on the part of a genito-urinary specialist were the precipitating factors in the suicide of an adult patient. Chronic masturbation is caused by "an irritation in the prostatic urethra"; "it is a real disease" (page 15). Although he warns against exaggerated beliefs regarding the results of masturbation, Dr. Hühner feels it necessary to point out that, "strictly speaking," the memory of patients with this condition is not really impaired. The treatment, which gives "excellent results," is prostatic massage and silver nitrate.

The bibliography is in part antiquated, and contributions on the subject since 1914 are not included.

Neuropsychiatry should perhaps not aspire to treat the majority of the conditions included in this book. Education in psychiatry, however, should succeed in drawing the attention of specialists to the broad aspects of human behavior, which do not allow the problems of disorders of the sexual function to be reduced to a question of one or two orifices.

A Study of Masturbation and the Psychosexual Life. By John F. W. Meagher. Second edition. Price, $2. Pp. 130. New York: William Wood & Company, 1929.

There was a time when masturbation was regarded by physicians as an important cause of nervous and mental ills. When its great frequency and relative harmlessness were discovered, the reaction against the previous misconceptions of deleterious effects of masturbation went so far that little attention has been given to the investigation of psychopathologic problems connected with it. Today there

is a definite need for a sound and intensive monographic treatment of the subject of masturbation. One is reminded of this need when reading the title of Dr. Meagher's book: "A Study of Masturbation and the Psychosexual Life." The book itself, however, falls short of this need, or even of stating clearly the main problems connected with the subject.

The following points are emphasized by Dr. Meagher: Infantile masturbation is practically universal. During adolescence it is more common in boys than in girls; in adult life it is more common among women than among men. While not abnormal in young children, it is always abnormal in adults. Masturbation does harm chiefly in mental and moral spheres, less in the physical sphere. Sympathetic and encouraging treatment is preferable to censorious and punitive measures.

The author states in his introduction that he has omitted all case histories because he thought that they would not add to the general principles he evolves. This lack of case histories would not be so important if the author had not also omitted statements of any concrete facts and situations. Instead, his book contains a surprising number of indefinite general statements and commonplaces. On one brief page (p. 14) one finds the following platitudes: "In fact attitude has much to do with all our reactions in life"; "For after all motherhood and fatherhood are sex situations"; "Difference of opinion as to whether a situation or thing is good or bad in great part depends on attitude"; "What one must develop is a normal, healthy attitude in regard to sex matters." Throughout the book are frequent references to the literature on the subject, or rather the names of famous investigators, which are dragged in without any attempt to present their ideas coherently and without much connection with the text. There is the same type of lack of facts and concreteness when the author deals with literature as when he deals with his subject. The following statements are typical: "As Ivan Bloch said, hunger and love rule the world"; "As Stekel says, the sex life of man, too, is most important." The reader gains little from this pseudo-erudition, which without any discernible necessary connection heaps on one page (p. 65) these names: Lallemand, Simon, Voltaire, Leitner, Hippocrates, Erb, Fürbinger, Jones, Stanley Hall, Healy, Moll, Jung, von Hug Helmuth, White, Kempf, "and others," "and many others."

It does not become apparent what the author's general point of view is concerning masturbation, nor is it made clear what type of definite facts he considers important in the examination and treatment of or advice to persons for whom masturbation is a problem. One gets the impression that the author has a moral rather than a scientific attitude toward masturbation. Witness his definition of masturbation: "As ordinarily practiced, masturbation is an act to produce a pure form of sensory pleasure bought at the expense of high moral tone" (page 63), and the statement that "the struggle for such people (psychopathic types) to be pure or to win a suitable marital object is too great" (page 84). This is even more apparent when he defines normal coitus as "legitimate coitus" (page 97). He implies that masturbation alone can cause serious nervous disorders (page 90), although this—important—point is not clearly developed. There is an index to authors and subjects, but no bibliographic data to help the reader who is not already informed to orient himself in this important field which the author sketches only imperfectly.

DIE OPTISCHE ALLESTHESIE. STUDIEN ZUR PSYCHOPATHOLOGIE DER RAUMBILDUNG. By GEORG HERRMANN and OTTO PÖTZL. Price, 28 marks. Pp. 302. Berlin: S. Karger, 1928.

Herrmann and Pötzl describe a pathologico-anatomic observation which they call "optic allesthesia" (imaginary local signs within the visual space — things which are seen occasionally, under the influence of central changes, not in their actual place). Patients have the right conception as to space, form and size, but see things actually in a different place. Beyer made observations on himself during an attack of migrainous scotoma, and a similar experience has been described by Ernst Freund. Optic allesthesia was compared with other optic disturbances of

optic motor and agnostic nature, and the entire work of investigation done in the Vienna Clinic of Julius Wagner-Jauregg.

The optic picture is transferred so that things left or right, above or below, are exchanged within the visual space. This has been recognized as a counter (contrasting) phase of tactile allesthesia. In order to differentiate optic from tactile allesthesia and to establish a name based on the accompanying symptom-complex, the authors called it "optic allesthesia." As far as it concerns things which appear suddenly like hallucinatory phases and remain unobserved in their right place, the content of these phases resembles "physical air-reflections." The authors called this "fata morgana" of the visual space. The symptom was thoroughly examined and investigated in a number of clinical cases, and the coincidence of two conditions (old parietal focus, alcoholic hallucinosis) had been suspended by phases of a tachitoscopic exposition of complex image groups which belong to this symptom. For this occurrence two conditions are necessary and these must react together: (1) a reaction which reduces central vision or injures it partially and (2) a suspension of certain directing components of the total complex of simultaneously fixed reactions, which the occipital convexity exercises on the area striata.

A case is reported in which the center of the visual field was temporarily suspended and showed an imaginary exchange of left and right attributable to a combination of an older softening focus in the left occipital region and a new focus proceeding from the right occipital convexity.

The coincidence of these two conditions made it possible to compare optic allesthesia and the spinally conditioned tactile allesthesia, which was experimentally demonstrated by Dusser de Barenne who combined two chief conditions: (1) a unilateral blocking of centripetal sensory spinal cord tracts by separating the spinal cord unilaterally; (2) a local hyperexcitation of the posterior horn, caudally and simultaneously, a unilateral separation (induced by slight local strychninization).

The similarity between optic and tactile allesthesia was summed up thus: A partial blocking of the centripetal sensory tracts and an extinction of specific factors take place as a sequel of a special suspending action within locally determinable graduated centers. Further investigations concerned the type and the localization of this suspending action and the comparison of optic allesthesia with other related symptoms of parieto-occipital focal diseases. There are numerous morphologic-physiologic parallels between the finer structure and the performances of the area striata, especially the identity of trophic and projective relations between the area striata and corpus geniculatum laterale of von Monakow, with the retina projection and double supply according to von Wilbrand and Henschen. It is shown that the retina projection is dependent on directing reactions exercised by the parieto-occipital convexity on the area striata and in turn on the corpus geniculatum laterale.

Finally there result conceptions concerning the total structure of those systems which create the system of coordination for the adaptation and upkeep of space impressions. It is shown that they are partly identical with the extended system of the bundles of His and that the commissure formation in the cerebrum is to be considered a continuation and extension of the system of the bundles of His. These relations were thoroughly investigated in their developmental history and were followed up comparatively to phylogenesis.

THE PSYCHOLOGY OF THE ADOLESCENT. By LETA S. HOLLINGWORTH. Price, $2.50. Pp. 227. New York: D. Appleton & Company, 1929.

This book by an associate professor of education at Teachers College, Columbia University, has grown out of a series of lectures. It is primarily intended for parents and teachers, but the author states that for years "students in the later years of adolescence" have attended these lectures and have shown great interest in them. It is no small achievement to write a book which can be profitably read at the same time by postadolescents, teachers and parents. The author has

succeeded in this to a remarkable extent, and one might add that physicians, too, might find here in readable form "a verbal formulation of the chief facts about those ambiguous years of life when the girl or boy is neither child nor adult, but a mixture of both." The book contains no startling new facts, if it contains any new facts at all, but it sets forth the problems of adolescence in the setting of contemporary life with a great deal of human insight and evidently a sound knowledge of the main scientific achievements.

The first chapter, "What Is Adolescence?" gives a brief survey of the subject. After a chapter on "Pubic Ceremonies," there follows one on "Psychological Weaning" in which the problems of emancipation from home are well discussed. Chapter IV, "Seeking Self-Support," contains a good statement of the questions of vocational guidance in adolescence. The problem of sex is discussed under the heading "Mating." The last three chapters deal with adolescent philosophy and religion ("Achieving a Point of View"), the growth of the personality ("Finding the Self") and the relationship of adolescence to maturity ("The Meaning of Maturity").

The author's sympathetic description of the often preventable minor tragedies of adolescence will be instructive to the many people who have forgotten their experiences during those years. Under the heading "Anxieties Due to Growth," for example, are discussed such problems as are involved in the size of shoes, the first shaving and the first menstruation. Without giving the appearance of erudition, the book contains a great deal of knowledge, which may not be sufficiently appreciated by those who look for complicated scientific terminology.

Although the book is far above the majority of the present wave of "mental hygiene" literature, it nevertheless contains a few of the errors so commonly found there. On the whole, mental tests — or rather, the Binet-Simon test — are overrated. Auto-erotism is treated with the perversions and not sufficient space is devoted to it. After all, it is one of the important problems of adolescence, and it needs more than one sentence. There is an unwarranted optimism that "most serious aberrations could be prevented" by application of the principles of mental hygiene in childhood. Like many psychologists dealing with broad problems of human behavior, the author is weakest where data of psychopathology are concerned. "Adolescent insanity" is an obsolete term and the explanations of schizophrenia on a basis of normal psychology are superficial, and unfortunately not correct. Otherwise one could prevent schizophrenia frequently, as the mental hygiene enthusiasts proclaim.

With these minor qualifications, the book can be heartily recommended as one of the best popular expositions of the problems of adolescence available today. There is an interesting bibliography including scientific literature and fiction.

THE PSYCHOLOGY OF MENTAL DISORDERS. By ABRAHAM MYERSON. Price, $1.40. Pp. 135. New York: The Macmillan Company, 1928.

Both in title and in format this little book reminds one of Bernard Hart's: "The Psychology of Insanity," which first appeared in 1912. Dr. Hart ably and successfully presented the psychology of mental disease from the psychoanalytic point of view. Since the appearance of his book, which went through a number of editions, there has been a gap in psychiatric literature for a brief presentation of the psychology of mental disease not based exclusively on psychoanalysis. Dr. Myerson, who declares himself as a "conservative in psychopathology," by writing this book has emphasized the existence of this gap, rather than filled it.

After a brief survey of the social problem of mental disease, the mind-body problem is briefly, but hardly adequately, discussed. Chapters 2 to 4 deal with the main symptoms and manifestations of the major and minor psychoses. The keynote of his "psychology" of these disorders seems to be that there is no psychology of mental disease, which hardly agrees with the title. He states, for example, in the paragraph on mood alterations (page 26) that "pathological mood of the type which leads to the insane hospital arises either out of an inborn personality disorder, or else out of disease processes, it does not arise out of 'pure' psychological

situations." The lay reader will hardly be satisfied if two intangible and unknown factors are presented to him as the "psychology" of these disorders. Paranoia and pellagra are discussed together in one brief paragraph. The psychopathology of the psychoneuroses may in the author's opinion be all discarded some day, to be replaced by a "biochemistry of the minor mental disorders." Throughout the book there is a tendency not to take stock in the facts at hand, but to point to hidden organic causes; e. g., in the statement: "In manic-depressive psychosis the main change is in mood, on some organic basis we do not understand" (page 95). It is not astonishing, then, that his discussion of psychopathic personalities is particularly inadequate. "The Germans" did not, as the author erroneously believes, merely change the words "moral imbecile" to "psychopathic personality," nor did "the Americans, to show their psychiatric insight, add a milestone to progress by coining the label 'constitutional inferior'" (p. 103). Many of the laymen whom Dr. Myerson wishes to enlighten know a great deal more than that nowadays about the development of these important conceptions connected with the names of Koch, Ziehen, Kraepelin and Adolf Meyer.

The fifth chapter deals with psychoanalysis, the sixth with crime, the seventh with the problem of heredity. The discussion of psychoanalysis is flippant, inaccurate in details and on the whole not informing. Freud is pronounced a great man, but practically all he teaches or is supposed to teach is rejected without any discrimination between what has proved valuable and what has not.

Although the book is readable as a whole, its usefulness is greatly impaired by the lack of chapter headings, table of contents or index.

DE L'ANGOISSE À L'EXTASE. ÉTUDES SUR LES CROYANCES ET LES SENTIMENTS. TOME SECOND. SENTIMENTS FONDAMENTAUX. By DR. PIERRE JANET, Membre de l'Institut, Professeur de Psychologie au Collège de France. Travaux du laboratoire de psychologie de la Salpêtrière. Price, 80 francs. Pp. 697. Paris: Librairie Félix Alcan, 1928.

In the first volume of this series "Un délire religieux, la croyance," Janet presented a study of intellectual functions and particularly of beliefs. In the present volume he reports an analytic study of the feelings or sentiments underlying the character of beliefs. The book is divided into three main parts with a number of subdivisions. Part I discusses various theories of the nature of feelings and reviews in detail the pathologic feeling of emptiness (vide). From a study of many examples and a review of the literature, Janet points out that mental activities may be divided into two categories, which he calls primary and secondary, similar to the distinction between reflex and voluntary activity. Primary acts are more or less habitual and automatic reactions to immediate situations; secondary activities are of a higher order and represent additions to primary action through the operation of memory functions. Analysis leads him to conclude that the feeling of emptiness and "still more the state of emptiness depends on the suppression of a host of secondary acts, of a crowd of echoes and harmonics which ordinarily accompany normal action." These conclusions are reached from a comparison of the acts and behavior of patients during such pathologic states of feeling with those of the same persons after recovery or during more or less complete remissions. With this as a foundation for his study, Janet proceeds to analyze other sentiments, both normal and pathologic.

Part II, the regulation of action, deals with sentiments of pressure and effort; states of morose inaction and fatigue; melancholic conditions and sadness; states of elation and joy. Part III, the organization of the feelings, includes the emotions proper; the beatitudes, and the evolution of the feelings.

The material is presented in the masterly style that one is accustomed to expect from Pierre Janet and contains an enormous mass of carefully studied and digested observation which is made readily available through an excellent index. The bibliography, also indexed, is excellent. The work is a real contribution to this obscure subject and should be read by every one interested in psychopathology.

INTELLIGENT LIVING. By AUSTEN F. RIGGS. Price, $2. Pp. 230. New York: Doubleday, Doran & Company, 1929.

A biologic way of looking at things is at once in evidence in this book. The human infant is "a little animal who has practically no frontal-lobe activity, no intelligence, but many modifiable instinctive reactions." The child from 3 to 7 years of age is a savage, varying greatly from his compeers in the strength of his instincts, curious and suggestible, with a beginning understanding of himself and others. From the eighth to the twelfth years, in a state near barbarism, the instincts are controlled, and intelligence has so advanced as to be the best means of approach. Then up to the age of 17 is the stage of primitive civilization, when ideals are built up and when wishful thinking is replaced by skeptical and careful observation. All of these steps parallel the myelinization of different nerve fibers and cannot be hurried.

"And with the growth up the scale, as intelligent planning increases, we find the culmination in ethical purposes. We find that our happiness lies in so fitting ourselves into the scheme of things as to win 'the love of our friends' and 'the approval of our community.' Ethical strivings are just as clearly evolutionary products as are the tropisms of insects."

Failure in life may come from several causes, but the one most worth immediate attention in the patients who come to the psychiatrist is mismanagement of the instincts through lack of specific information, or through misinformation. Many people, for instance, have been taught that some emotions are good and others bad. To get ahead, to get over a neurosis, a patient needs correct information about his emotions and his real purpose in life. The author discusses friends, the married, the unmarried and the training of the child with these points in view. His practical suggestions include making obedience come first for the young child, with reasons coming second; a sharp differentiation between work and play; the unemotional application of authority; the extension of certain kindergarten methods into more advanced grades. He concludes with a summary of his philosophy of a balanced life, in which rest and play and intelligent choice can bring about a cultured and a happy existence in adult years.

It would be hard to find a book for patients and physicians to read that is as pleasing and as well founded in principle and fact. It is not by any means an inclusive guide to the psychoneuroses.

THE NEW PSYCHOLOGY OF THE UNCONSCIOUS. By C. W. VALENTINE, M.A., B.Sc., PH.D., Professor of Education, University of Birmingham. Price, $1.60. Pp. 162. New York: The Macmillan Company, 1929.

This compact volume represents the author's additions and improvements to his original "Dreams and the Unconscious" first published in 1921. Here he deals with such fundamental phases as mental conflict and repression, the psychology of dreams, the practical aspects of mental analysis and the ethical nature of sublimation and moral eduction, dispatching each with a brief discussion. The points of departure are, of course, chiefly views expounded by Freud, and the criticism is of the sweeping generalizations manifest in many of his writings. Valentine adds to the freudian interpretation of dreams the concept that in the dream the completion of a process begun in waking life may be realized. He removes some objections to freudian psychology by pointing out that the psychoanalytic methods and interpretations are merely unfamiliar examples of recognized fundamental laws.

The book is a clear and concise summary of the views of those he chooses to call the freudians and neofreudians presented in correlation with orthodox psychology. He has the faculty of clarifying involved psychologic explanations by a rather ingenious definition and relatively simple illustration. He is almost diagramatic in his ability to reduce to simple understandable terms. The book is perhaps a little more adaptable to the student than to the lay reader, and it gives many leads for further reading. It is of particular value as an introduction to the newer psychology for the student who finds many present-day writings involved and controversial.

SELECTED READINGS IN PATHOLOGY FROM HIPPOCRATES TO VIRCHOW. Edited by ESMOND R. LONG, Professor of Pathology, University of Chicago. Price, $4.00. Pp. 301. Springfield, Ill.: Charles C. Thomas, 1929.

In this volume the author has compiled a series of excerpts from the classics of pathology taken from Hippocrates to Virchow, that is, during the known history of medicine. It is interesting and fascinating reading and the entire profession is indebted to the author for the consummation of this enterprise and for the excellent selection that he has made. The book itself is well prepared with readable type and the illustrations are excellent.

THE ARCHIVES OF NEUROLOGY AND PSYCHIATRY is published by the American Medical Association to stimulate research in the field of diseases and disorders of the nervous system, and to disseminate knowledge in this department of medicine.

Manuscripts for publication and correspondence relating to the editorial management should be sent to Dr. T. H. Weisenburg, Editor-in-Chief, 1930 Chestnut St., Philadelphia, or to any other member of the Editorial Board. Books for review should be addressed to Dr. Weisenburg. Communications regarding subscriptions, reprints, etc., should be addressed, ARCHIVES OF NEUROLOGY AND PSYCHIATRY, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on condition that they are contributed solely to the ARCHIVES OF NEUROLOGY AND PSYCHIATRY. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones of illustrations will be supplied by the Association when the original illustrations warrant.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index Medicus, published by the American Medical Association. This requires, in order given: name of author, title of article, name of periodical, with volume, page, month—day of month if weekly—and year. A complete list of abbreviations for standard periodicals, together with a full discussion of the style of the A. M. A. publications, appears in The Art and Practice of Medical Writing, a comprehensive book on the preparation of medical manuscripts, published by the American Medical Association. Price, $1.50.

Matter appearing in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY is covered by copyright, but, as a rule, no objection will be made to its reproduction in reputable medical journals if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY or in any of the other publications issued by the Association, will not be permitted.

Authors will receive one hundred reprints free; additional reprints may be obtained at cost.

The ARCHIVES OF NEUROLOGY AND PSYCHIATRY is published monthly. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75, including postage. Single copies, 85 cents, postpaid.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

OTHER PERIODICAL PUBLICATIONS
of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Covers all the medical sciences and matters of general medical interest. Illustrated. Annual subscription price (two volumes): Domestic, $7.00; Canadian, $8.50; foreign, $8.50. Single copies, 35 cents.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the publication of advanced, original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $5.40; foreign, $5.75. Single copies, 75 cents.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. Presents pediatrics as a medical science and as a social problem. It includes carefully prepared collective abstracts based on recent pediatric literature, abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and full abstracts of the literature on these two subjects, transactions of the important dermatological societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF SURGERY—Monthly. Devoted largely to the investigative and clinical phases of surgery, with monthly reviews on orthopedic and urologic surgery. Well illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

ARCHIVES OF PATHOLOGY—Monthly. A periodical devoted to the publication of original contributions in the field of pathology, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

ARCHIVES OF OPHTHALMOLOGY—Monthly. Includes original articles on diseases of the eye, abstracts from foreign and domestic literature, book reviews, transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

QUARTERLY CUMULATIVE INDEX MEDICUS—Quarterly. A complete subject and author index to the worth-while current medical literature of the world. Issued four times a year. Second and fourth volumes bound for permanent reference. Subscription price, calendar year: Domestic, $12.00; Canadian, $12.50; foreign, $12.75

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn St. CHICAGO

CONTENTS

THE CEREBELLUM: A NEW CLASSIFICATION OF THE LOBES BASED ON THEIR REACTIONS TO STIMULATION. AUBREY T. MUSSEN, M.D., BALTIMORE 461

CORTICAL ANOMALIES, VENTRICULAR HETEROTOPIAS AND OCCLUSION OF THE AQUEDUCT OF SYLVIUS. JAMES W. KERNOHAN, M.B., CH.B., ROCHESTER, MINN. 465

POSTVACCINAL (COWPOX) ENCEPHALITIS: A CLINICOPATHOLOGIC REPORT OF A CASE. GEORGE B. HASSIN, M.D., CHICAGO, AND J. C. GEIGER, M.D., SAN FRANCISCO 481

HYPEROSTOSIS AND TUMOR INFILTRATION OF BASE OF SKULL ASSOCIATED WITH OVERLYING MENINGEAL FIBROBLASTOMA. N. W. WINKELMAN, M.D., PHILADELPHIA 494

COCCIDIOIDAL GRANULOMA: REPORT OF TWO CASES SIMULATING TUMOR OF THE SPINAL CORD. CARL W. RAND, M.D., LOS ANGELES 502

PARALYTIC DEMENTIA: THE LOCALIZATION OF SPIROCHAETA PALLIDA IN THE BRAIN. CHARLES G. AARS, M.D., PARAMARIBO, DUTCH GUIANA 512

STUDIES IN EPILEPSY: WILLIAM G. LENNOX, M.D., AND MARGARET B. ALLEN, B.S., BOSTON:

IX. THE SUGAR CONTENT OF THE SPINAL FLUID 520

X. THE CHLORIDE CONTENT OF THE BLOOD AND SPINAL FLUID 525

THE KAHN PRESUMPTIVE PROCEDURE WITH SPINAL FLUIDS. ELIZABETH B. MCDERMOTT, ANN ARBOR, MICH. 531

CLINICAL NOTES:

BROWN-SÉQUARD SYNDROME AS A MANIFESTATION OF SYPHILITIC NEURORECURRENCE: REPORT OF A CASE. JUI-WU MU, M.D., AND CHESTER N. FRAZIER, M.D., PEIPING, CHINA 536

QUANTITATIVE ESTIMATION OF TOTAL PROTEIN OF CEREBROSPINAL FLUID: A MODIFICATION AND IMPROVEMENT OF A PREVIOUSLY DESCRIBED METHOD. G. ALEXANDER YOUNG, M.D.; A. E. BENNETT, M.D.; J. M. CHRISTLIEB, M.D., AND JOHN T. MYERS, M.D., PH.D., OMAHA 542

NEWS AND COMMENT 548

OBITUARIES:

C. FLOYD HAVILAND 548

HERMAN HENRY HOPPE 548

ABSTRACTS FROM CURRENT LITERATURE 549

SOCIETY TRANSACTIONS:

GERMAN NEUROLOGICAL SOCIETY 575

NEW YORK NEUROLOGICAL SOCIETY 595

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY 603

BOOK REVIEWS 608